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ABSTRACTS OF WORLD MEDICINE

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ABSTRACTS OF WORLD MEDICINE

UNDER THE DIRECTION OF
HUGH CLEGG, M.A., M.D., F.R.C.P., Editor, *BRITISH MEDICAL JOURNAL*

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It is the aim of this journal to provide the reader with abstracts of all important articles appearing in medical periodicals published in every part of the world, and in this way to enable him to keep in touch with new developments throughout the whole field of medicine and in each of its special branches, including those aspects of surgery which are of particular concern to the physician.

More than 1,600 periodicals are surveyed, from which are selected for abstracting those papers which appear to make some useful contribution to the sum of medical knowledge or experience. Each paper is abstracted in sufficient detail to indicate to the general reader the nature and value of that contribution and to enable the specialist to assess its importance in relation to his own work and to decide whether the original article should be read in full. The author's own summary or an editorial summary published with the original article may occasionally be reproduced if it is suitable for these purposes, and the title and reference alone may be published in order to draw attention to a review article or other type of paper which cannot readily be abstracted.

The abstracts in each issue are grouped in sections according to subject and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together. The titles of papers written in languages other than English are given both in translation and in the original form. The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals*, as modified by *ISO Recommendation R4: International Code for the Abbreviation of Titles of Periodicals* (International Standards Organization, 1957), and in *World Medical Periodicals* (Second Edition, World Medical Association, 1957). The transliteration of authors' names from the Cyrillic alphabets is in accordance with *ISO Recommendation R9: International System for the Transliteration of Cyrillic Characters* (International Standards Organization, 1955).

Explanatory or critical comments by the abstracter or editor are enclosed within square brackets.

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ABSTRACTS OF WORLD MEDICINE

VOL. 28 NO. 5 NOVEMBER, 1960

Pathology

1106. **Influence of the Pituitary on the Erythropoietic Principle Produced in the Kidney**
S. OSNES. *British Medical Journal* [*Brit. med. J.*] **1**, 1153–1157, April 16, 1960. 10 figs., 13 refs.

This study from the University of Oslo describes the continuation of the work previously reported by the author (*Brit. med. J.*, 1959, **2**, 650; *Abstr. Wld Med.*, 1960, **27**, 346) on an erythropoietic principle (kidney factor or K.F.) produced by the kidney. In a series of experiments on mice and rats it was shown that production of K.F. is stimulated by the pituitary gland, the substance responsible being identical with the adrenocorticotrophic hormone, but acting by an extra-adrenal mechanism. *A. W. H. Foxell*

1107. **Physical Activity in Experimental Cholesterol Atherosclerosis of Rabbits**
S. D. KOBERNICK and G. NIWAYAMA. *American Journal of Pathology* [*Amer. J. Path.*] **36**, 393–409, April, 1960. 6 figs., 39 refs.

In experiments reported from Sinai Hospital and Wayne State University College of Medicine, Detroit, Michigan, 96 New Zealand white rabbits were kept for 58 to 189 days on a high-cholesterol diet. Every day they were exercised for 10 to 20 minutes either in a manually operated plywood drum or in an ingeniously devised electrical drum in which an electrostimulator compelled them to run and to rotate the drum about 50 times a minute. A similar number of rabbits were fed cholesterol, but allowed to remain sedentary. At the end of the experiment the animals were killed, complete necropsy performed, the aorta fixed in formalin, and the adventitia meticulously removed with every trace of adventitial fat. The extent of atherosclerosis was carefully estimated and sketched. Small representative portions of the aorta were removed for histological examination and the entire remainder was subjected to alcohol–ether extraction. The lipid content of the aorta was determined by the method used for serum.

In the first series of experiments, performed with the manually operated drum, the differences in extent of atherosclerosis between the exercised and the sedentary animals were not sufficiently clear-cut to be considered significant. The experiments performed with the mechanical treadmill showed, however, that in adequately exercised, cholesterol-fed rabbits the extent of atherosclerosis produced in the aorta was definitely less than that in sedentary control animals. There was, however, no distinct correlation between the serum levels of cholesterol, cholesterol esters, and lipid phosphorus or the serum cholesterol:lipid-phosphorus ratio and exercise, nor could a correlation be established between these values and the extent of aortic atherosclerosis.

Z. A. Leitner

1108. **Intimal and Medial Lipids in Human Aortas**
E. B. SMITH. *Lancet* [*Lancet*] **1**, 799–803, April 9, 1960. 2 figs., 9 refs.

An investigation was carried out at the Middlesex Hospital Medical School, London, to determine: (1) whether analysis of intimal and medial lipids would reveal any identity with individual lipoprotein fractions; (2) the chemical changes occurring in intima and media with lesions of increasing severity; and (3) whether the data indicated a different origin for the lipid in different types of lesion. Lipids were analysed in 56 tissue samples from 22 aortas obtained at necropsy from cases of myocardial infarction, other heart conditions, cerebral haemorrhage, carcinoma, diabetic gangrene, syphilitic atherosclerosis, pneumonia, and steatorrhoea. The sex and age distribution of the patients was as follows: 7 males aged 25 to 59 and 5 aged 60 and over; 4 females aged 52 to 59 and 6 aged 60 and over.

The author's findings are summarized as follows. "In normal areas the concentration of lipid in intima and media is similar, but its composition differs in the proportions of free and esterified cholesterol, in the proportions of cholesterol and phospholipid, and in the proportions of the lecithin and sphingomyelin components of the phospholipid.... There is no correlation between the severity of atherosclerosis and the lipid content of normal patches of intima or media. There is, however, a significant correlation between age and the normal intimal concentration of total lipid ($P<0.02$) and of cholesterol ($P<0.01$). In lesions of increased severity both intimal and medial lipids increase in a uniform manner.... In more advanced lesions there is an increase in the proportion of sphingomyelin in the intimal phospholipid, and in the necrotic lesions it may account for 70 to 80% of the phospholipid." *G. Clayton*

1109. **A New Diagnostic Test in Amyloidosis (Preliminary Communication)**
S. JARNUM. *Lancet* [*Lancet*] **1**, 1007–1008, May 7, 1960. 2 figs., 10 refs.

During studies at Bispebjerg Hospital, Copenhagen, of the plasma volume of patients with amyloidosis the author noted a discrepancy between the value obtained

with the azovan-blue test and that obtained with the radioactive-iodine-labelled albumin method. He states that in the normal subject the plasma volume as determined by both methods is identical and the disappearance rates from the blood do not differ within the first hour after injection. A case of amyloidosis is described in which the apparent plasma volume as determined with azovan blue exceeded that with iodized albumin by 46%, the subsequent disappearance rate also being appreciably higher. At 45 minutes after injection the iodized albumin concentration had decreased by 7% and that of azovan blue by 30% as compared with the values 15 minutes after injection.

On the basis of these and similar findings in 2 other patients a new diagnostic test for amyloidosis is suggested. A blood sample (A) is taken 4 minutes after the injection of azovan blue and another sample (B) 15 minutes after the injection. If the dye concentration of B is less than 80% of A amyloidosis is probably present. The author states that even better results can be obtained by using the two techniques; if the plasma volume with azovan blue exceeds that with iodized albumin by more than 10% the patient probably has amyloidosis. It is considered that these tests may turn out to be more specific than the Congo red test, since the rapid removal of azovan blue can be due only to an abnormal non-circulating protein with a dye-binding power which is many times that of the ordinary plasma globulins and perhaps nearly as high as that of albumin. The abnormal globulin could be in or close to the capillary wall. Were it intravascular it would not affect determination of plasma volume with azovan blue. In a case of myelomatosis with a high concentration in the plasma of an abnormal gamma globulin the plasma volume determined with azovan blue was correct.

G. Clayton

HAEMATOLOGY

1110. **The Cellular Composition of Inflammatory Exudates in Human Leukemias**
D. R. Boggs. *Blood* [*Blood*] **15**, 466–475, April, 1960. 7 figs., 11 refs.

The author reports the results of an examination of the cellular character of infammatory exudates in patients with leukaemia. Inflammation was induced by Rebuck's procedure of scraping the epithelium on the volar surface of the forearm until the papillary layer of the corium was reached and then applying a drop of diphtheria toxoid and covering the area with a coverslip. This was changed after 3, 6, 12, and 24 hours, dried, stained by Giemsa's method, mounted, and examined. Tests were performed on 4 patients with chronic myelocytic, one with probable chronic monocytic, one with probable chronic eosinophilic, 10 with chronic lymphocytic, 8 with acute myeloblastic, and 10 with acute lymphoblastic leukaemia. Control tests were carried out on 7 healthy subjects and 6 patients with metastatic carcinoma but with normal leucocyte counts.

In the control subjects the pattern of cellular response was fairly uniform; segmented neutrophil granulocytes predominated in the 3- and 6-hour exudates, but by 12 hours polymorphonuclear and mononuclear leucocytes were usually present in equal numbers. By 24 hours the mononuclear cell was predominant. Amongst the patients with chronic leukaemia the cellular response was generally normal except that the number of band forms and metamyelocytes was increased. The granulocyte content of the induced inflammatory exudate correlated well with the number of circulating mature neutrophil cells and metamyelocytes, immature leukaemic cells not being found. The major abnormalities were found in the cases of acute leukaemia, in which acellular exudates were frequently encountered and the macrophage response was deficient, particularly in cases of acute lymphoblastic leukaemia. Immature leukaemic cells were rarely seen in the exudates. No differences were noted in the granulocytic response between the acute lymphoblastic and myeloblastic forms of leukaemia.

Infection was more frequently encountered amongst the patients with acute leukaemia and a decreased granulocytic response. Deficient phagocyte production appears to be one at least of the defects leading to depressed bacterial defence in acute leukaemia.

A. Ackroyd

MORBID ANATOMY AND CYTOLOGY

1111. **The Relation between Left Atrial Hypertension and Lymphatic Distension in Lung Biopsies**
D. Heath and P. Hicken. *Thorax* [*Thorax*] **15**, 54–58, March [received May], 1960. 5 figs., 9 refs.

The transient basal horizontal lines frequently seen in chest radiographs during periods of cardiac failure (Kerley's lines) have been attributed to oedema of the connective tissue together with lymphatic distension. When present they are accompanied by a left atrial blood pressure of more than 24 mm. Hg. In a study reported from the University of Birmingham biopsy material obtained at operation from the lingula in 20 cases of mitral stenosis of rheumatic origin was examined to see whether pulmonary lymphatic distension could be related to pulmonary venous hypertension. In all cases the left atrial or pulmonary arterial "wedge" pressure was measured.

The mode of assessment of lymphatic distension was found to be important. No correlation could be found between the left atrial blood pressure and the size of isolated lymphatics as measured in histological sections. When a bronchus and its accompanying pulmonary artery were surrounded by dilated lymphatics, however, a state of "pulmonary lymphangiectasis" was said to exist and the authors found that there was good correlation between the presence of pulmonary lymphangiectasis and a pulmonary venous pressure of more than 30 mm. Hg with an associated pulmonary arterial pressure of more than 60 mm. Hg. They therefore conclude that this is a reliable histological method of assessing lymphatic distension and that this is related to the presence of severe pulmonary venous hypertension in cases of heart failure.

G. J. Cunningham

1112. **An Electron Microscopic Investigation of the Jejunal Epithelium in Sprue**

R. S. HARTMAN, C. E. BUTTERWORTH JR., R. E. HARTMAN, W. H. CROSBY, and A. SHIRAI. *Gastroenterology* [*Gastroenterology*] **38**, 506–516, April, 1960. 10 figs., 11 refs.

It has been estimated that the thickening of the villi of the small intestine in tropical sprue may reduce its absorptive surface to 25% of normal. This in itself is insufficient to account for the whole of the absorption defect, and the present study was carried out at the Walter Reed Army Institute of Research, Washington, D.C., to examine the state of the epithelium, especially of the microvilli forming the brush border. Biopsy with a Crosby intraluminal suction biopsy capsule was performed on 7 patients with tropical sprue. A brief outline of the method used for the preparation of specimens for electron microscopy is given and the normal electron-microscopic picture of the human jejunum is illustrated and discussed.

In 2 cases of acute untreated tropical sprue there was a striking paucity of epithelium and the villi usually bore no intact covering. The crypts were lined with epithelium, but cytoplasmatic vacuolation, fragmentation of the intercellular membranes, abnormal shape and position of the nuclei, and leucocytic infiltration were frequently seen. The microvilli were sometimes normal in size and number and sometimes short or sparsely distributed or both. The apical cell boundary was usually intact. In 2 cases in which non-specific treatment only had been given the appearances resembled those in 3 cases in which the anaemia had been corrected by treatment, although there was still demonstrable malabsorption. There were fairly widespread areas of cell breakdown, but the structure of the tissue was usually an orderly palisade of cells. The only disturbance of the brush border observed was the frequency with which the apical cell membrane was broken. The findings in one case of non-tropical sprue are also briefly mentioned.

The conclusion reached is that the gross reduction of villus surface together with the loss of epithelial covering of the remaining villi may reduce the total absorptive surface in acute tropical sprue to less than 5% of normal.

F. Hillman

1113. **Studies of Celiac Disease. II. The Apparent Irreversibility of the Proximal Intestinal Pathology in Celiac Disease**

C. E. RUBIN, L. L. BRANDBORG, P. C. PHELPS, H. C. TAYLOR JR., C. V. MURRAY, R. STEMLER, C. HOWRY, and W. VOLWILER. *Gastroenterology* [*Gastroenterology*] **38**, 517–532, April, 1960. 16 figs., 22 refs.

In a previous communication from the University of Washington School of Medicine, Seattle, (*Gastroenterology*, 1960, **38**, 28; *Abstr. Wld Med.*, 1960, **28**, 92) the authors presented evidence to show that the proximal intestinal lesions in coeliac disease and idiopathic sprue are identical in nature. In order to study the reversibility of this lesion 114 suction biopsies were taken from 32 patients with coeliac disease or idiopathic sprue, 7 of whom had been treated with a gluten-free diet for one month to 5 years, and from a similar number of appropriate control subjects, 13 of whom were healthy and the remainder suffering from various gastrointestinal disorders. The age incidence and criteria of diagnosis in the group with coeliac disease are specified and technical details concerning histological processing are given.

A simple quantitative method for estimating the length of epithelial surface by means of random epithelial counts was used and gave an average value of 71 in the control subjects and 37 both in coeliac disease and in sprue. In an additional group of 6 patients who gave only an indefinite history of coeliac disease and were well and free from steatorrhoea while taking a gluten-containing diet the average count was normal. The age of the patient, the duration of the illness, and the clinical state could not be correlated with the severity of the intestinal histological lesion. Specimens taken from children before and after treatment with a gluten-free diet for some time showed some improvement in the mucosal pathology, but none occurred in adults on a similar regimen in spite of striking clinical improvement. In cases of coeliac disease the brush border on the luminal surface of the intestinal absorptive cells was intact. Loss of the brush border and vacuolation of the epithelium were most frequently seen in the mid-portion of the tips of broadened villi. It is suggested that delay in the proliferation of fresh cells from the depth of the crypts possibly allows these cells to remain an excessively long time in position before being shed and that these " rotten " cells may reflect a decrease in the number of crypts. The possibility of a genetic influence is mentioned in connexion with cases affecting a mother and daughter, a father and daughter, and a pair of male twins.

In discussing their findings the authors point out that specimens taken from different sites at the same time or repeated biopsies may reveal widely different pictures. In most cases, however, the histological lesion appears to be irreversible. To explain the lack of correlation between the histological and clinical pictures it is suggested that: (1) the total extent of involved bowel may be more important than the degree of severity of the lesions; (2) the essential changes may not be revealed by ordinary light microscopy; or (3) the histological changes may be secondary to an underlying metabolic defect. It is claimed that the data presented " offer further support for the contention that childhood celiac disease and adult idiopathic sprue are but different phases of the same hereditary illness ".

F. Hillman

1114. **The Histopathology of Chronic Ulcerative Colitis and its Pathogenic Implications**

M. B. GOLDGRABER, J. B. KIRSNER, and W. L. PALMER. *Gastroenterology* [*Gastroenterology*] **38**, 596–604, April, 1960. 10 figs., 24 refs.

This paper reports a study of 124 cases of ulcerative colitis, collected from the records of the University of Chicago, in which bowel surgery, necropsy, or both were performed. A total of 2,000 conventional histological slides were reviewed and the results tabulated in an attempt to throw light on the pathogenesis of the disease.

The clinical, radiological, and proctoscopic data and the gross appearance of the tissues at the time of operation or necropsy were also reviewed and the findings are outlined.

There was little correlation between the gross appearance of the colon by inspection or radiography and its histopathology, microscopy often revealing the disease in what had appeared to be a normal segment of colon. There was also little relationship between the duration of symptoms and the severity of the disease. The commonest microscopical findings were ulceration and "pseudopolyps". Ulceration was seen in 85% of cases and its presence in the other cases could not be ruled out, though it was not obvious in the material reviewed. "Pseudopolyps" were found in 65% of patients, the term being used in its widest sense to include anything protruding from the inner surface of the gut wall, including mucosal tags as well as inflammatory and adenomatous polypoid lesions.

"Cryptitis" was found in only 20% of cases. It is not considered to be important in the mechanism of ulceration in ulcerative colitis because ulceration was often seen in areas where no evidence of cryptitis was found and in most cases of cryptitis the collection of inflammatory cells did not damage the integrity of the mucosa. Granulomata with and without giant cells were found in 35 and 40% of cases respectively. These are described and illustrated and it is suggested that they indicate a hypersensitivity mechanism. Other features supporting the theory of a hyperimmune reaction were the finding of tissue eosinophilia in 40% of cases and the frequent finding of vascular thrombosis, lymphatic dilatation, and perivascular infiltration [incidence not given], all these vascular changes being also frequently found in experimental hypersensitivity reactions. Acute vasculitis was present in only one case and endothelial desquamation in 3, so that neither of these conditions would appear to play a part in the mechanism of ulceration in ulcerative colitis. No case of "aganglionic" colon was seen, nor was there any suggestion of defective cellular regeneration.

Other findings recorded include fistulae and sinuses in 15%, abscesses in 15%, and perforation into the peritoneal cavity in 10%. Mucosal atrophy was seen in 23% of cases, and 26% showed buried epithelium (which has been implicated in the development of malignant change). Adenoma was found in 26% and carcinoma in 19% of cases. The factors associated with neoplastic change are to be discussed in a further paper.

I. Berkinshaw-Smith

1115. **Human Cardiac Conduction Tissue Lesions**

G. LUMB and R. S. SCHACKLETT. *American Journal of Pathology* [*Amer. J. Path.*] **36**, 411–429, April, 1960. 15 figs., 22 refs.

At the Institute of Pathology, University of Tennessee, Memphis, the atrioventricular node and the bundle of His and its branches were carefully examined in a series of 260 human hearts obtained at necropsy, the object being to determine the relationship between the pathological changes in this area and the clinical findings. Changes in the conduction tissue were found in 35 cases. In 25 of these death had been sudden, but in 13 there were pathological changes elsewhere which were sufficient to cause death; in the remaining 12 no satisfactory cause of death could be found "outside the heart", and definite lesions of the conduction tissue were present. Electrocardiographic (ECG) tracings were available in 26 of the 35 cases, and 19 of them revealed lesions of the conduction tissue. On pathological examination the lesions were found to be more widespread than was suggested by the ECG findings. There was only one case in the series showing marked pathological changes but no ECG evidence of injury to the conduction fibres, probably because only a few fibres are necessary to maintain conduction.

J. B. Wilson

1116. **The Relation of Age and Blood Pressure to Atheroma in the Pulmonary Arteries and Thoracic Aorta in Congenital Heart Disease**

D. HEATH, E. H. WOOD, J. W. DUSHANE, and J. E. EDWARDS. *Laboratory Investigation* [*Lab. Invest.*] **9**, 259–272, March–April, 1960. 2 figs., 4 refs.

The incidence and severity of atherosclerosis in the pulmonary arteries were studied in relation to age, the mean blood pressure in the pulmonary artery, the pulmonary blood flow, and the hypertensive structural changes in the small pulmonary arteries in 65 cases of congenital or acquired heart disease seen at the Mayo Clinic.

Of a group of 21 cases of congenital heart disease characterized by pulmonary stenosis, atheroma was absent from the elastic pulmonary arteries in each of the 19 cases with normal or diminished arterial blood pressure and pulmonary blood flow; the small muscular arteries were also normal. However, in 2 cases of Fallot's tetralogy with abnormally high pulmonary arterial blood pressure and flow both elastic-artery atheroma and hypertrophy of the small muscular arteries were present.

Of a group of 22 patients with congenital heart disease who had had pulmonary hypertension since birth, all except one out of 16 aged 3½ years or more showed plaques of atheroma, the atheroma being severe in patients over 13 years. Older patients in this group with confluent atheroma in the pulmonary arteries tended to have the more severe grades of hypertensive pulmonary vascular disease and diminished pulmonary blood flow.

In the remaining 22 cases in the series heart disease was associated with acquired pulmonary hypertension. Atheroma was present in the 21 patients aged 20 years or more, and in 16 the lesions were confluent. In this group there was no relationship between the severity of the pulmonary atheroma and the grade of hypertensive structural changes in the small pulmonary arteries. The latter was related to the level of the pulmonary arterial pressure, but the severity of the atheroma appeared to be more closely related to age and possibly to pulmonary blood flow.

Atheroma occurred in the thoracic aorta in the second decade of life in most cases and in the first part of the aorta from childhood in all cases. The authors conclude that the factors of pulmonary hypertension,

increased pulmonary blood flow, and associated haemodynamic stresses are related to the development of pulmonary atheroma in congenital heart disease.

H. Caplan

1117. **Metaplasia of the Bronchial Mucosa in Cases of Bronchial Carcinoma.** (Über Metaplasien der Bronchialschleimhaut bei Fällen von Bronchialcarcinom)
F. E. STRUWE. *Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie* [*Beitr. path. Anat.*] **122**, 57–79, 1960. 12 figs., bibliography.

In post-mortem material from 17 cases of bronchial carcinoma available at the Institute of Pathology of the University of Freiburg im Breisgau the author has studied the mucous membrane of the complete bronchial tree with the aid of a dissecting microscope, from the trachea to the small bronchial branches so far as technically possible. Areas which aroused suspicion of being metaplastic by virtue of a grey, dull appearance were excised and examined histologically in serial sections. Of the 17 cases studied, 6 showed areas of metaplasia, while one showed only the earliest stages of this alteration. The remaining 10 cases aroused no suspicion of metaplasia on macroscopic examination. No particular distribution of the areas of metaplasia could be established. The author is therefore unable to draw any conclusion from this study regarding the relationship of metaplasia to bronchial carcinoma.

G. Loewi

1118. **The Pathologic Effects of Smoking Tobacco on the Trachea and Bronchial Mucosa**
K. P. KNUDTSON. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **33**, 310–317, April, 1960. 6 figs., 18 refs.

At the Veterans Administration Hospital, Seattle, specimens of bronchial and tracheal mucosa obtained post mortem from 100 subjects ranging in age between 23 and 85 years were examined and histories of the smoking habits of these individuals was obtained. A control group of 10 subjects under 10 years of age was used for comparison. The mucosa was removed from the cartilage plates by sharp dissection and examined by the "Swiss-roll" technique. The classification of changes in the bronchial epithelium proposed by Auerbach *et al.* (*New Engl. J. Med.*, 1957, **256**, 97; *Abstr. Wld Med.*, 1957, **22**, 5) was followed and the classification of smoking habits of Wynder and Graham (*J. Amer. med. Ass.*, 1950, **143**, 329; *Abstr. Wld Med.*, 1950, **8**, 636) adopted. The incidence of abnormalities in the tracheal and bronchial epithelium was higher in smokers than in non-smokers and in older than in younger age groups. No excessive frequency of abnormal bronchial epithelium could be found in (*a*) town dwellers as compared with persons living in rural areas, or (*b*) those employed in occupations recognized as hazardous for lung cancer as compared with persons in other occupations.

[This paper is interesting in that it suggests that basal-cell hyperplasia, squamous metaplasia, and atypical proliferative metaplasia represent successive stages in the development of cancer of the lung. Previous workers have regarded basal-cell hyperplasia as the likely precancerous lesion. The main difficulty in accepting either view lies in the fact that such proliferative changes are common in the trachea (as in the present study), a situation in which carcinoma is very rare. It is noteworthy that hyperplastic changes were also discovered frequently in cigar or pipe smokers. In contrast with Auerbach, but in agreement with other workers (Cunningham and Winstanley, *Ann. roy. Coll. Surg. Engl.*, 1959, **24**, 323; *Abstr. Wld Med.*, 1959, **26**, 260), no relationship was found between smoking habits and the presence of carcinoma-*in-situ*. The "Swiss-roll" technique for such a study is open to criticism as tangential cuts are frequent and it is therefore often difficult to eliminate artefacts.] *G. J. Cunningham*

1119. **Emphysema, Soot, and Pulmonary Circulation—Macroscopic Studies of Aging Lungs**
C. P. ODERR. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 1991–1998, April 30, 1960. 9 figs., 11 refs.

A study of the relationship between parenchymal soot deposit and emphysema is reported in this paper from the Veterans Administration Hospital and Tulane University School of Medicine, New Orleans. The lungs of 200 patients who had died from diseases other than pulmonary tuberculosis were injected by various pressure methods and fixed in the inflated state, thin slices of pulmonary tissue being then taken for macroscopic examination. A definite relationship was found between the presence of soot deposits in the lung parenchyma and developed areas of emphysema. The author discusses the probable way in which the emphysema arises, and shows that there is first of all fenestration of the alveolar walls and dilatation of the alveolar ducts. Precapillary vessels protrude into some alveoli, and the possible part they play in subsequent dynamic changes is outlined. A semi-shunt mechanism at the periphery of the lobes was demonstrated in the injection specimens.

J. B. Wilson

1120. **Cerebral Vascular Lesions and Peptic Ulceration**
J. B. DALGAARD. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **69**, 359–370, April, 1960. 5 figs., 28 refs.

The investigation herein described forms part of a comprehensive study of neurogenic peptic ulceration as seen at necropsy and is based on the findings in 4,317 cases in which necropsy was performed in the Departments of Pathology and Forensic Medicine at the Universities of Copenhagen and Aarhus, Denmark, and Bergen, Norway. In exactly 100 cases (2·3%) there were primary cerebrovascular lesions and oesophageal, gastric, or duodenal ulceration. Acute peptic ulceration was found in 67 cases and chronic ulceration in 33. No aetiological relationship could be proved in cases of chronic ulceration, but it appears probable that cerebral vascular lesions are the commonest single cause of acute peptic ulceration as seen at necropsy. Such acute neurogenic lesions may occur within 12 hours, but are found mostly a few days after the apoplexy.

A. W. H. Foxell

Microbiology and Parasitology

1121. **Further Experience with Hemagglutination in Viral Hepatitis**

L. M. MORRISON, R. E. HOYT, M. LEVINE, M. ROSENTHAL, R. L. HOLEMAN, and M. R. STEVENS. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **33**, 461–466, April, 1960. 7 refs.

In an earlier paper Morrison and Hoyt (*J. Lab. clin. Med.*, 1957, **49**, 774; *Abstr. Wld Med.*, 1957, **22**, 424) reported that serum from patients with infective hepatitis agglutinated erythrocytes of the *Macaca rhesus* monkey and suggested that the reaction was of significant clinical value and might also be used as a screening test for blood donors. In this further paper the results obtained by applying the test to 1,710 sera from patients with viral hepatitis, patients with other diseases, and healthy controls are presented. Of 1,334 control sera 15% gave a positive result compared with 90% of sera from 95 patients with acute viral hepatitis and jaundice and 72% of sera from 196 similar patients without jaundice. The sera of only 2 (5%) of 40 newborn babies with non-viral jaundice resulting from congenital atresia of the bile ducts gave a positive reaction. In 7 (35%) of 20 cases of infectious mononucleosis the result was positive. The authors claim that this test can be used to differentiate viral from obstructive jaundice. They point out that in a number of cases several samples of blood had to be tested before a positive result was obtained. It is not yet possible to say whether haemagglutination results from the direct action of the virus upon the monkey erythrocytes, from the activity of viral antibodies, or from the presence of some abnormal blood component during the course of infective hepatitis.

Janice Taverne

1122. **Hemagglutination Test for Viral Hepatitis with Special Reference to Nonspecific Reactions**

E. R. JENNINGS and C. HINDMARSH. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **55**, 519–521, April, 1960. 4 refs.

The present authors report a study of the specificity of the rhesus erythrocyte agglutination test [see Abstract 1121] in relation to viral hepatitis. A total of 41 specimens of serum from patients with hepatitis and 206 from other patients, including 16 with liver disease, were tested for rhesus-cell agglutinins. Of the 41 sera from patients with hepatitis, 32 (78%) were positive compared with 2 (12%) of 16 sera from cases of other liver disease. However, 70% of sera from medical students and laboratory workers were also positive. It was at first thought possible that antibodies to monkey erythrocytes had arisen after vaccination against poliomyelitis, but no correlation was found. Instead, the number of positive sera could be related to age. None of 10 samples of serum from newborn infants was positive; of 23 sera from children in hospital, 15 (65%) were positive, and of 60 from normal adults 36 (72%) were positive. Fewer sera from geriatric patients were positive (6 out of 49 (12%)); it is suggested that this would account for the lower percentage found among patients with liver disease, since they were all from older age groups. The test does not appear to be specific for viral hepatitis.

Janice Taverne

1123. **Immunization of Infants with Formalinized Poliomyelitis Vaccine (Salk Type)**

I. SPIGLAND and N. GOLDBLUM. *Pediatrics* [*Pediatrics*] **25**, 812–821, May, 1960. 6 figs., 18 refs.

The authors of this paper from the Virus Laboratory, Tel Aviv-Yaffo, Israel, state that during the last decade children aged 6 months to 3 years represented the age group in Israel which was most prone to paralytic poliomyelitis, the incidence of the disease being highest in infants aged 6 to 12 months. They report the results of an extensive study undertaken to determine at what age immunization with Salk vaccine is effective. A total of 594 infants aged 1 to 6 months from various socio-economic groups were given either two 1-ml. injections of Salk-type vaccine 3 weeks apart or three injections of 1 ml. each, the last two being given 7 and 21 days respectively after the first. The vaccines used were of high potency, as judged from guinea-pig antigenic extinction titres. The infants were divided into 3 groups according to age at primary immunization: Group A, 1 and 2 months of age; Group B, 3 and 4 months; and Group C, 5 and 6 months. All antibody responses were determined at the age of 6 months.

Before immunization maternal antibodies could be detected in 87 to 94% of infants at birth, in 50% at the age of 3 months, and in 11 to 16% at age 5 to 6 months. After primary immunization antibody developed in an appreciable percentage in all three groups, but the greater the age at primary immunization the better the response. Conversion rates and antibody titres were higher in infants in Group C than in Group B, and these in turn were higher than in Group A. No appreciable difference was observed between Groups A and B in antibody response as a result of the different immunization schedules, but in Group C post-primary conversion rates for poliomyelitis virus Types 1, 2, and 3 were 71%, 98%, and 53% respectively after the two-injection course and 90%, 100%, and 85% respectively after three injections. The best response in all groups was to Type-2 antigen, the response to Type 1 being less good and to Type 3 the poorest. The presence of maternal antibody seemed to interfere with active production of antibody. In infants without demonstrable antibody after primary immunization a booster dose, given about 6 months after the last inoculation, produced excellent responses for Type-1 and Type-2 antigens, but a considerable number failed to respond to Type-3 antigen. Responses were independent of the age of the infants and of the presence or absence of maternal antibody at primary immunization.

A. Ackroyd

Pharmacology and Therapeutics

1124. **Amphetamine, Secobarbital, and Athletic Performance. II. Subjective Evaluations of Performances, Mood States, and Physical States**
G. M. SMITH and H. K. BEECHER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 1502–1514, April 2, 1960. 4 refs.

In an earlier investigation (*J. Amer. med. Ass.*, 1959, **170**, 542; *Abstr. Wld Med.*, 1960, **27**, 94) it was found that the performance of athletes was improved after administration of 15 mg. of amphetamine per 70 kg. body weight and was impaired by 100 mg. of secobarbital (quinalbarbitone) per 70 kg. The authors have now studied the subjective responses to these drugs of the same 57 athletes, who received by mouth at a suitable interval before an athletic performance 7, 14, or 21 mg. of amphetamine or 50 or 100 mg. of quinalbarbitone per 70 kg. or a placebo. It was previously known that the maximum effect of amphetamine occurred after 2 to 4 hours and of quinalbarbitone after 30 minutes to 2 hours. Each subject was asked to reply to a questionary of 17 items concerning physical feelings and capacity and of 81 items concerning mental effect and moods, and to state whether there was any improvement or impairment in actual performance. Performance was improved after 14 mg. of amphetamine per 70 kg.; it was impaired after 100 mg. and not modified by 50 mg. of quinalbarbitone per 70 kg. There were improved feelings of strength, endurance, and elation after amphetamine and also after the smaller dose of quinalbarbitone. The larger dose of the latter caused intoxication, " deactivation ", and distortion of judgment. *V. J. Woolley*

1125. **Amphetamine, Secobarbital, and Athletic Performance. III. Quantitative Effects on Judgment**
G. M. SMITH and H. K. BEECHER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 1623–1629, April 9, 1960. 4 figs., 18 refs.

In this further investigation of the effect of amphetamine and quinalbarbitone on athletic performance 15 good swimmers were given 14 mg. of the former or 100 mg. of the latter per 70 kg. body weight or a placebo before a 100- or 200-yard (90 or 180-metre) swim. Performance time and the subject's judgment of it and of the performance itself were recorded. Amphetamine resulted in a slight improvement in performance, but caused the subject to undervalue it. After quinalbarbitone there was marked impairment of performance, but the subject believed that it was improved. The errors of judgment were more marked when the subject swam alone than when he had two companions. An analysis of the replies to a questionary of 16 items relating to subjective effects of the drugs showed that most of the subjects thought, wrongly, that quinalbarbitone enhanced their fitness, but observed no change with amphetamine. *V. J. Woolley*

1126. **An Analysis of the Analgesic Effect of *dextro*-Propoxyphene Hydrochloride, Phenaglycodol, and Aspirin Combination (Darvo-tran)**
E. SETTEL. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **6**, 512–517, Sept., 1959 [received May, 1960]. 6 refs.

In a highly controlled, double-blind study of the analgesic effect in 50 patients presenting a variety of acute pain situations of three drug combinations: (1) drug C (*dextro*propoxyphene-acetylsalicylic acid-phenaglycodol) proved to be the most effective of the three; (2) drug B (*dextro*propoxyphene-acetylsalicylic acid) was demonstrated to be 14% less effective in reducing pain; and (3) drug A (placebo) was much the least effective. By submitting the clinical data obtained to the highly objective statistical transformation of ridit analysis, a comprehensive interpretation of results could be formulated.

Side effects were of little clinical significance, consisting mainly of occasional constipation, nausea, drowsiness, and mild gastric distress. These effects were distributed about equally between drugs B and C. Statistically, they were negligible with drug A, the placebo.—[Author's summary.]

1127. **A Potential New Therapy for Febrile Seizures: Preliminary Report on Development of *N*-Phenylbarbitone**
J. G. MILLICHAP. *British Medical Journal* [*Brit. med. J.*] **1**, 1111–1112, April 9, 1960. 1 fig., 6 refs.

The treatment of febrile seizures in infants and young children with phenobarbitone and aspirin is successful in only about 50% of cases, while phenytoin sodium is totally ineffective. Experiments were therefore carried out at the Massachusetts General Hospital, Boston, to find a more potent anticonvulsant for use in such cases.

Febrile seizures were induced in young albino mice by a diathermy method and drugs in various doses tested for their antipyrexial and anticonvulsant activity, 5 to 10 animals being used at each dose level. Aspirin either failed to retard the rate of temperature rise or, in toxic doses, increased the severity of the febrile seizure. Phenytoin was also ineffective. Phenobarbitone prevented the febrile seizure, but large depressant doses were required. Of 60 new drugs tested, *N*-phenylbarbitone (" pyrictal ") was the most potent anticonvulsant. Sedation was of minimal degree; tremor and clonic movements were observed only with sublethal doses.

N-phenylbarbitone was also given to epileptic patients in an average dose of 17 mg. per kg. body weight. A reduction in the incidence of fits of 75% or more was obtained in 8 out of 15 patients with major seizures and 9 out of 10 patients with minor types of epilepsy. *N*-phenylbarbitone was found to be antipyretic in a group of 7 febrile children. Doses of 20 mg. per kg. administered from the onset of a febrile illness prevented febrile seizures in a group of 12 patients. Side-effects

were seen only with continuous medication; these consisted in restlessness, anorexia, and sedation. Further evaluation of the drug against febrile seizures, hyperpyrexia, and minor epilepsy is considered to be warranted.
Norval Taylor

1128. **The Pharmacology of Neuromuscular Blocking Agents in Man.** [Review Article]
F. F. FOLDES. *Clinical Pharmacology and Therapeutics* [*Clin. Pharmacol. Ther.*] **1**, 345–395, May–June, 1960. Bibliography.

1129. **Further Studies of the Influence of Carbon Dioxide on Neuromuscular Blocking Agents in the Cat**
J. P. PAYNE. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 202–205, May, 1960. 4 figs., 7 refs.

The influence of carbon dioxide on the neuromuscular blocking properties of benzoquinonium, laudexium and two tropane derivatives has been studied. The action of benzoquinonium is antagonized by carbon dioxide; the effect of tropane derivatives is enhanced and that of laudexium is unchanged. No satisfactory explanation for these different observations is as yet available.—[Author's summary.]

1130. **Drugs Which Stimulate Affective Behaviour. 2. Comparison of the Analeptic Effect of D-Amphetamine, Bemegride with Amiphenazole, Methylphenidylacetate, Iproniazid (Micoren) and RP8228**
A. B. DOBKIN. *Anaesthesia* [*Anaesthesia*] **15**, 146–153, April, 1960. 31 refs.

A comparative study of the analeptic effects of D-amphetamine, bemegride, amiphenazole, methylphenidylacetate (" ritalin "), iproniazid, " prethcamid ", and " RP 8228 " was carried out at the University of Saskatchewan College of Medicine, Saskatoon. The drugs were administered intravenously to counteract the effects of a standard intravenous dose (25 mg. per kg. body weight) of sodium thiopentone, cross-over experiments being carried out with each drug on 10 mongrel dogs.

It was found that all the drugs immediately and effectively reversed the apnoea induced by thiopentone. D-Amphetamine produced a highly significant reduction in both the recovery time and the time to ambulation. Prethcamid and RP 8228, the two newest drugs, also significantly accelerated recovery, and the author considers that these merit clinical trial. *Mark Swerdlow*

1131. **Some Experiences with a New Anabolic Steroid (Methandrostenolone)**
G. L. FOSS. *British Medical Journal* [*Brit. med. J.*] **1**, 1300–1305, April 30, 1960. 10 figs., 5 refs.

The effects of an anabolic steroid (methandrostenolone) on 7 children, 2 adolescents, and 4 adults suffering from delayed growth have been studied at the Endocrine Clinics, United Bristol Hospitals. Anorexia associated with respiratory tract infections was the cause of dwarfism in 3 of the children, and one child had a ventricular septal defect; the cause of dwarfism in the remaining 3 children was not apparent. One of the adolescents was suffering from ovarian dysgenesis and the other from gonadotrophic deficiency due to a pituitary tumour. Of the adults, all females, 3 were suffering from malignant neoplasms and one was healthy.

Methandrostenolone stimulated growth in all patients; there was an increase in appetite with considerable gain in weight. In the early stages, when the daily dose was 2·5 mg. per kg. body weight, marked androgenic effects were observed, but with a daily dose of approximately 0·5 mg. per kg. only minor androgenic effects occurred. The steroid did not affect the menstrual rhythm of the healthy adult. *R. M. Todd*

1132. **The Use of L-Lysine Monohydrochloride in Combination with Mercurial Diuretics in the Treatment of Refractory Fluid Retention**
A. L. RUBIN, N. SPRITZ, A. W. READ, R. A. HERRMANN, W. S. BRAVEMAN, and E. H. LUCKEY. *Circulation* [*Circulation*] **21**, 332–336, March, 1960. 2 figs., 8 refs.

In view of the frequency of intolerance to ammonium or calcium chloride given in association with mersalyl in the treatment of refractory oedema the use of L-lysine monohydrochloride as an alternative was investigated in 14 patients at Bellevue Hospital (Cornell University Medical College), New York. All the patients had oedema due either to congestive heart failure or cirrhosis and all were refractory to previous treatment with bed rest, digitalis, and diuretics. L-Lysine monohydrochloride was given in doses of 10 g. 4 times daily for 2 to 5 days, at first alone and then together with a mercurial diuretic. Body weight, urine volume and electrolyte content, and plasma electrolyte levels and *p*H were measured during an initial control period and the two treatment periods.

In all cases there was an increase in plasma and urinary chloride content during the administration of L-lysine monohydrochloride, but no significant loss of weight. No hyperpnoea or other acidotic symptoms occurred. When a mercurial diuretic was then given a significant loss of weight occurred in every case, with a return of the plasma chloride level towards normal. Potassium chloride was given by mouth to prevent potassium depletion in this period. The only side-effect produced was diarrhoea, and there was no evidence of renal or haematopoietic toxicity.

The authors conclude that L-lysine monohydrochloride is a useful adjuvant to the treatment of refractory fluid retention, but advise that it should be used only in hospital to avoid the serious effects of a severe metabolic acidosis. *Gerald Sandler*

1133. **Efficacy of Silicone Antifoam Agents in the Control of Pulmonary Edema**
R. C. BALAGOT, M. S. SADOVE, and R. M. REYES. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 197–200, March–April, 1960. 6 refs.

Experiments were carried out at the Illinois College of Medicine, Chicago, designed to determine the efficacy of silicone antifoam preparations in the control of pulmonary oedema. Rabbits were exposed in a specially constructed plastic chamber to aerosols of Compound

5526, " alevaire ", Compound 5708A, or Compound 5708B, each aerosol being given to a group of 16 animals. (The exact composition of these compounds is given in a table.) After exposure for 30 minutes each animal was given an injection of 2 mg. of adrenaline (1 in 1,000 concentration) into an ear vein. Thereafter the rabbits were exposed continuously until death or for one hour, when they were killed. The lungs were then examined to determine the degree of oedema and the ratio of lung weight to body weight.

The findings suggest that silicones are very effective in preventing or controlling pulmonary oedema and that alevaire compares favourably with Compound 5526, these two being superior to the other agents tested. The implications of the findings are discussed.

Mark Swerdlow

1134. **The Cardiovascular–Respiratory Effects of a New Xanthine Derivative in Chronic Pulmonary Emphysema and in Mitral Stenosis**

F. Barrera, J. C. Dominguez, R. L. Changsut, G. G. Regalado, L. Arias, and J. Faura. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **239**, 487–491, April, 1960. 11 refs.

Eleven cases of " pure " mitral stenosis and 8 cases of advanced pulmonary emphysema were studied during cardiac catheterization, at rest and 30 minutes after intravenous administration of 0·1 to 0·2 gm. of a new xanthine derivative Ro 1–8239. The drug increases alveolar ventilation, reduces physiological dead space, arterial pCO_2, $V_D:V_T$ ratio and increases arterial blood *p*H. These changes are interpreted as action on pulmonary circulation probably associated with bronchodilatation. The drug produced a drop in systemic and pulmonary pressures at the end of 15 and 30 minutes. It decreases all resistance and increases cardiac output. These changes are due to vasodilatation, both systemic and pulmonary.—[Authors' summary.]

1135. **Animal and Human Studies on Ferrous Fumarate, an Oral Hematinic**

M. C. Berenbaum, K. J. Child, B. Davis, H. M. Sharpe, and E. G. Tomich. *Blood* [*Blood*] **15**, 540–550, April, 1960. 4 figs., 6 refs.

Investigations into the toxicity of ferrous fumarate, given by mouth, as compared with the sulphate, succinate, and gluconate are reported. In mice the relative acute oral toxicities were: fumarate 1, succinate 1·1, gluconate 2, and sulphonate 2·7, while the relative emetic activities in cats were: fumarate, succinate, and gluconate 3 and sulphate 4. Massive doses of ferrous sulphate or gluconate produced marked irritant and toxic effects in the stomachs and livers of rabbits, while the effects after the succinate and fumarate were negligible. The growth rates of male, but not female, rats treated for 12 weeks with high doses of the four iron compounds were less than normal, but on a low dosage of the fumarate or gluconate (50 mg. Fe per kg. body weight daily) the depression of growth was not significant and histological examination of the major organs revealed no abnormalities which could be attributed to the drugs. In repairing an iron deficiency in rats the fumarate was as effective as iron dextran given intramuscularly or the other iron compounds given orally. Haematological improvement was observed in all but one of 23 patients with hypochromic anaemia treated with ferrous fumarate (" fersamal ") in doses of 200 mg. Fe daily. The tablets were acceptable to all. The refractory patient was also refractory to ferrous sulphate and gluconate.

A. Ackroyd

1136. **Simplification and Improvement in Estimating Drug Dosage and Fluid and Dietary Allowances for Patients of Varying Sizes**

A. M. Butler and R. H. Richie. *New England Journal of Medicine* [*New Engl. J. Med.*] **262**, 903–908, May 5, 1960. 6 figs., 21 refs.

Although it is customary to state doses of drugs and requirements of food and fluids in terms of body weight, such values are applicable only to adults within a limited range of weight, there being no linear relationship between the dosage required to maintain a required blood level and the body weight. To compensate for this the dosage per unit weight must be reduced as weight (or age) increases; this practice necessarily entails a wide margin of variation and considerable inconvenience.

The authors call attention to the long-recognized and well-documented observations (*a*) that the therapeutic dosage of drugs and fluid requirements, together with such physiological variables as blood and plasma volume, renal blood flow, glomerular filtration rate, and caloric requirements, have a more or less constant proportionality to surface area, and (*b*) that surface area is approximately proportional to weight to the exponent 0·7, and can therefore be estimated with ease (coefficient of variation approximately 8%). They then demonstrate the wide variations in dosage of a number of common drugs which results from the different methods of estimation and different standards in use at a number of U.S. and Canadian paediatric clinics. They emphasize the simplicity of prescribing on the basis of dosage per square metre of body surface and suggest that the relations between safe and effective dosage and tolerance can be discerned more readily than when the dosage is based upon the body weight. By the same token the approximate proportionality of caloric requirements to surface area permits the recommendation of caloric and protein allowances on the basis of a single value per square metre (for example, 1,700 Cal. and 30 g. protein basic allowance) rather than an allowance per kg. or per pound body weight which diminishes as weight and age increase.

Statements regarding fluid allowances or requirements can also be expressed as a single value per unit of surface area or as multiple values per unit weight. For healthy children and adults the margin between maximum tolerance and minimum requirement is so wide as to make theoretical accuracy irrelevant; this is not the case in early infancy and in patients whose homeostatic functions have been impaired by illness or trauma. The authors hence urge the adoption of surface area as the basis for adjusting fluid allowance to the size of the patient.

R. H. Cawley

Chemotherapy

1137. **The Sensitivity of Hemolytic Staphylococci to a Series of Antibiotics. II. A Three-year Progress Report**
R. G. PETERSDORF, M. C. ROSE, H. B. MINCHEW, W. R. KEENE, and I. L. BENNETT JR. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **105**, 398–412, March, 1960. 12 figs., 18 refs.

The authors report the results of tests carried out at the Johns Hopkins University School of Medicine, Baltimore, on the sensitivity of 300 strains of staphylococci, including 150 from patients with clinical infections, 50 from carriers with recent infections, and 100 from asymptomatic carriers, to penicillin, erythromycin, chloramphenicol, tetracycline, neomycin, bacitracin, oleandomycin, sigmamycin, ristocetin, novobiocin, kanamycin, vancomycin, and leucomycin. They compare the results with those of similar tests carried out 3 years previously. A tube dilution technique was used, with determination of bacteriostatic and bactericidal end-points; disk sensitivity tests and the Blair and Carr method of phage typing were also carried out.

In general, strains isolated from patients with clinical infections were more resistant than those obtained from asymptomatic carriers, with strains isolated from infected carriers falling between the two. This tendency was most marked with tetracycline and penicillin. Although many strains were resistant to penicillin, nearly 50% were sensitive to 50 units per ml. Vancomycin, kanamycin, ristocetin, erythromycin, and novobiocin were bactericidal, vancomycin being the most powerful, killing 50% of the strains at a concentration of 20 μg. per ml., whereas chloramphenicol, tetracycline, erythromycin, vancomycin, ristocetin, kanamycin, oleandomycin, novobiocin and leucomycin were bacteriostatic. Chloramphenicol inhibited 90% of the strains at a concentration of 10 μg. per ml. and tetracycline inhibited half the strains at 5 μg. per ml.

No increase in resistance to chloramphenicol or erythromycin during the past 3 years was noted, but some increase in resistance to penicillin was observed. However, since the latter was noted only at high concentrations it was probably an artefact. Organisms lysed by Phage 81 were uniformly resistant to high concentrations of penicillin and to tetracycline; they also tended to be slightly more resistant to most other agents. In general, the results of tube dilution tests were in good agreement with those of disk tests.

A programme for the treatment of staphylococcal infection acquired within or outside hospital is presented. It is suggested that severe systemic staphylococcal infection other than Phage-type 81 acquired outside the hospital should be treated with as much as 20 to 40 mega units of penicillin daily in conjunction with probenecid and that a second agent such as chloramphenicol or erythromycin should be added. When patients have clearly acquired the infection in hospital or the organisms are lysed by Phage 81 vancomycin or chloramphenicol should be used from the outset. The problem of overcoming staphylococcal infection does not lie in the discovery of new and more potent antibiotics, but in careful studies of the host's response to the infection.

Anne Tothill

1138. **The Susceptibility of Staphylococci to Chloramphenicol**
M. W. FISHER. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **105**, 413–423, March, 1960. 1 fig., bibliography.

A series of experiments on resistance to chloramphenicol were carried out on 24 strains of *Staphylococcus aureus*, 8 of which were sensitive and the remaining 16 were moderately or highly resistant to the drug. Mice were treated with 100 lethal doses of *Staph. aureus* in mucin adjuvant, which without treatment would be fatal in 24 hours. Groups of animals thus infected were treated with varying doses of chloramphenicol by mouth and the 50% curative dose was determined. It was found that staphylococci classed as resistant by tests *in vitro* were sensitive to chloramphenicol *in vivo*.

Further experiments were carried out with 23 selected highly resistant strains of staphylococcus, most of which required 100 μg. of chloramphenicol or more per ml. for inhibition *in vitro*. These strains were examined by agar dilution, broth dilution, and test disk methods. Only 2 of the 23 were resistant to more than 100 μg. of chloramphenicol per ml. *in vitro* by all these tests, but these strains were sensitive to treatment in experimentally infected mice. It was found that "false resistance" was obtained by the use of a heavy inoculum. In the disk test the 30-μg. disk gave more significant results than the 10-μg. disk, and it was concluded that a zone of inhibition of any size around the 30-μg. disk indicated possible susceptibility *in vivo*. The broth dilution test with a small inoculum seemed the most reliable, and complete inhibition by 100 μg. or less per ml. appeared to suggest that the strain might be susceptible *in vivo*. The results thus show that the degree of resistance reported in staphylococci may be exaggerated.

The author then reviews 52 publications and 2 unpublished works on the incidence of chloramphenicol-resistant staphylococci in man. He concludes that over a period of 9 years the average incidence of resistance among 31,779 strains was 9%, and that there was no significant difference between the incidence of resistant strains in institutions which did and those which did not make liberal use of chloramphenicol. There is no evidence of an increasing trend in the incidence of resistant strains. The rarity of true chloramphenicol resistance may be due to alteration in susceptibility occurring very slowly and to a limited degree, and to strains of decreased susceptibility being relatively short-lived both *in vitro* and in man; there is also some possibility that these two factors are related.

Anne Tothill

Infectious Diseases

1139. **Clinical Description of an Outbreak of Serous Meningitis Due to Coxsackie Virus.** (Клиника вспышки серозного менингита, вызванного вирусом Коксеки)

I. A. Kiričinskaja, G. F. Kolesnikov, and B. G. Krasnov. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 273–279, No. 3, 1960. 2 figs., 1 ref.

During the period June–August, 1958, an outbreak of serous meningitis occurred in Nikolaev, involving 230 patients. Of these, 206 were under the observation of the authors at three hospitals, 120 being boys, 82 girls, and 4 adults. The epidemic spread from a kindergarten to various creches in the town. Twelve of the children were under a year old, 121 between one and 6, 65 between 7 and 12, and the remaining 8 up to 16 years. The incubation period was 8 to 10 days. In 101 cases there was a fully developed meningeal syndrome and in 80 there were a few meningeal signs, while 25 patients had no meningeal signs, but had pyrexia, pharyngitis, and headache with vomiting.

In 60·6% of cases the pyrexia was biphasic, a first rise lasting one to 7 days being followed after an interval of 12 to 24 hours by a second rise of the same duration. Usually the pyrexial period lasted about 2 weeks, but in some cases a mild fever persisted for a longer period. Faucial hyperaemia was the rule and was present in 88% of the non-meningeal cases, and cervical adenitis was common. In addition to neck rigidity and positive Kernig's and Brudzinsky's signs, somnolence, and irritability many of the children exhibited asymmetry of the face and naso-labial folds, 6 had nystagmus, and 11 had a disturbance of the oculomotor or abducens nerve. The tendon reflexes of the lower limbs (and in 5 cases of the upper limbs) were unequal, and in 3 cases hypotonia of the muscles of the lower limbs was observed, but without loss of reflexes.

The cerebrospinal fluid (C.S.F.) showed pleocytosis, with a predominance of neutrophil granulocytes in most cases initially. The average number of cells was 100 to 300 per c.mm., but in some cases exceeded 1,000 per c.mm. By the beginning of the 2nd week lymphocytes predominated, the number of cells gradually falling to the end of the 4th week. The protein level of the C.S.F. in most cases was within normal limits, but in about one-third of the total it was moderately increased. The glucose content was in the region of 40 to 65 mg. per 100 ml. in 20 of the 22 cases in which it was estimated. There was a moderate rise in the erythrocyte sedimentation rate, but only in the first 11 days. Monocytosis was present in the peripheral blood, and after the 2nd week eosinophilia, the neutrophil count falling from 78% to 40% and the lymphocyte count increasing from 22% to 45%. The outcome was benign and there was no mortality. There were 3 cases of early and one of late recrudescence of symptoms.

A virus pathogenic to suckling mice was obtained from 18 out of 89 specimens of stools examined and from one specimen of C.S.F. The histological changes found in the young mice were typical of the changes found in infections by Coxsackie virus Group A.

L. Firman-Edwards

1140. **Rubella in Pregnancy: a Report on Six Embryos**

J. E. Gray. *British Medical Journal* [*Brit. med. J.*] **1**, 1388–1390, May 7, 1960. 13 figs., 9 refs.

Embryos from 6 cases in which pregnancy was terminated by hysterotomy because of rubella in the first trimester were examined in the Department of Anatomy, University of Durham. The embryos were fixed in Bouin's fluid and complete serial sections were studied. Foetal lesions, which were observed in 3 instances, included a patent interatrial foramen, lysis of the epithelial cytoplasm with cell disappearance in Corti's organs on both sides, and disintegration of the posterior part of the lens bilaterally. It is suggested that the foetal lesions are the results of cell destruction following invasion by rubella virus, like the cytopathogenic effects observed in tissue cultures infected by viruses.

D. Geraint James

1141. **Comparison of Activities of *iso*Citric Dehydrogenase and Glutamic–Oxalacetic Transaminase in Serum in Infectious Hepatitis**

O. Bodansky, M. K. Schwartz, S. Krugman, J. P. Giles, and A. M. Jacobs. *Pediatrics* [*Pediatrics*] **25**, 807–811, May, 1960. 1 fig., 8 refs.

A comparative investigation is reported of the serum *iso*citric dehydrogenase (S.I.D.) and the serum glutamic–oxalacetic transaminase (S.G.O.T.) levels in infective hepatitis. The S.I.D. activity was determined serially in 42 children who developed infective hepatitis, the time and extent of the rise in this value being compared with those in the S.G.O.T. level estimated concurrently in the same patients. The normal mean level of S.I.D. was 12·6 units, with a standard deviation of 3·8 units; the upper limit of normal was 22 units. In 8 out of 9 patients in whom clinical evidence of hepatitis developed after injection of virus the time of elevation and the height of the rise above normal were the same for both enzymes, but the S.G.O.T. level remained elevated longer and the relative rise to the upper limit of normal was greater for S.G.O.T. The authors prefer the determination of S.G.O.T. activity to that of S.I.D. activity in the study and diagnosis of hepatitis.

Winston Turner

1142. **Cat Scratch Disease**

W. B. Spaulding and J. N. Hennessy. *American Journal of Medicine* [*Amer. J. Med.*] **28**, 504–509, April, 1960. 1 fig., 12 refs.

The authors of this paper from the University and General Hospital, Toronto, discuss the findings in 83 cases of cat-scratch disease seen over a period of 4 years,

46 of which were observed personally. A history of contact with cats was almost invariable and of cat scratches in over half the cases. After an incubation period of 7 to 61 days a subacute granulomatous lymphadenitis occurred in various superficial lymph nodes, principally axillary (32 cases), cervical (17), or inguinal (15). In 26 cases the adenitis progressed to suppuration. Fever and constitutional symptoms were common but not invariable, and associated features were arthralgia, phlebitis, paronychia, erythema nodosum, splenomegaly, and encephalitis. In some cases there were changes in the blood, including leucocytosis, lymphocytosis, monocytosis, eosinophilia, and an increase in the erythrocyte sedimentation rate. The response to the lymphogranuloma venereum complement-fixation test was positive in 14 out of 39 patients, chiefly adults, and was negative in 120 adult controls. A skin test with antigenic material prepared from pus of a suppurating lymph node caused tuberculin-like (delayed-type) hypersensitivity in all patients and provoked an exacerbation of the infection in 3. The authors state that occasionally these are false positive and false negative reactions to the skin test. Antibiotics do not appear to influence the course of the disease, which may be due to a virus, although no aetiological agent was isolated in the present series. If gross suppuration occurs needle aspiration is recommended.

D. Geraint James

1143. **Observations on a Present-day Outbreak of Diphtheria**

M. J. KEHR, R. W. TANNAHILL, T. F. ELIAS-JONES, and L. WHITTAKER. *Public Health* [*Publ. Hlth* (*Lond.*)] **74**, 294–303, May, 1960. 10 refs.

The clinical features of 12 cases of diphtheria admitted to Chadwell Heath Hospital, Ilford, Essex, during a small outbreak in 1958 are discussed. In one case, that of a boy aged 7 which proved fatal, and in one admitted late in the disease with palatal palsy antibiotic treatment had been given at home for " sore throat ", and in neither was antitoxin given in hospital. In the fatal case diphtheria was not diagnosed until the appearance of unmistakable cardiac symptoms on the 11th day of disease, death occurring from toxic myocarditis the following day; this was the first case admitted during the outbreak. The second case admitted, that of a girl of 6, was of the typical " bull-neck " type—malignant diphtheria. Large doses of antitoxin were administered intravenously and intramuscularly, and after an episode of myocarditis with right bundle-branch block and one of palatal paralysis and right facial weakness the patient made a complete recovery. In this case the antibiotic given at home had been tetracycline and the throat swabs taken in hospital were negative. The third case admitted, with complete immobility of the palate and a history of sore throat 40 days previously, was believed to be the missed case of diphtheria which started the outbreak.

In the remaining 9 cases an attempt was made to discover whether antibiotic treatment in the acute stage was indicated in addition to antitoxin. The authors conclude that, except perhaps in laryngeal diphtheria, no discernible benefit accrues from administration of antibiotics in the acute stage of diphtheria [a view in which the abstracter concurs]. There is also the diagnostic problem set by antibiotic-masked diphtheria. Throat swabs are almost invariably negative and a correct diagnosis often depends on the observer's experience of diphtheria. Important points in diagnosis are pallor, listlessness, a rapid pulse in relation to the temperature, and the absence of a history of marked anginal symptoms. In acute cases in which diphtheria is suspected on these grounds massive doses of antitoxin should be given, preferably intravenously.

H. Stanley Banks

1144. **Diagnosis of Pertussis by Fluorescent Antibody Staining of Nasopharyngeal Smears**

P. DONALDSON and J. A. WHITAKER. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **99**, 423–427, April, 1960. 1 fig., 10 refs.

A method of diagnosis of pertussis by the staining of nasopharyngeal smears with fluorescent antibody is reported in this paper from the University of Texas Southwestern Medical School, Dallas. Specimens were obtained from children showing typical signs and symptoms of clinical whooping-cough, from patients with undifferentiated upper respiratory infections, and from healthy persons, and smears prepared and stained with fluorescent antibody specific for *Haemophilus* (*Bordetella*) *pertussis*. In the technique used rabbits were given an initial series of intraperitoneal injections of 29,000 million to 30,000 million *H. pertussis* organisms weekly for a period of 3 months; as the antibody titres were found to be low, similar intravenous injections were then given 3 times weekly for 3 weeks. The antiserum from a rabbit in which the titre reached 1:12,000 was conjugated with fluorescein and was found to be satisfactory for staining.

Out of 36 patients with pertussis, 31 yielded smears in which the aetiological agent was immunochemically stained in numbers that varied roughly from 3 organisms per 50 microscopical fields to hundreds of organisms per field. The aetiological agent could be identified in smears from all of 13 patients who had been treated with antibiotics for less than 48 hours, but from only 2 of 18 who had been treated for more than 48 hours. Among 8 persons who remained well but were exposed to siblings with pertussis, 2 were shown to be carriers of *H. pertussis* by this method, while 2 who later developed clinical whooping-cough also gave positive smears. Tests of 36 specimens from patients with other diseases or from healthy persons gave negative results in every instance.

The advantages of the method include its relative simplicity as compared with isolation of the organism on Bordet–Genjou medium, its rapidity, its specificity, and, probably, its high sensitivity.

R. G. Meyer

1145. **Pertussis: a Clinical Study**

S. KAUFMAN and H. B. BRUYN. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **99**, 417–422, April, 1960. 4 figs., 18 refs.

A review of 199 cases of pertussis is presented by the authors from the University of California Medical Center, San Francisco. Of these patients, 38% were under 6 months of age when admitted to hospital; 94 had a

history of contact with pertussis during the month before the onset of symptoms, 4 of the contacts being adults within the home. No significant correlation was found between susceptibility to pertussis and sex. The findings emphasized that child-to-child contact within the home is the most important way in which pertussis is acquired. Immunization, partial or complete, had been instituted in 31 cases before the onset of symptoms. The period of hospitalization averaged 17 days and was not affected by age, though children from whose throat *Haemophilus* (*Bordetella*) *pertussis* was cultured remained in hospital slightly longer than the rest. It is noted that an occasional case of parapertussis may have been included in the series as the two diseases are clinically indistinguishable. There is no cross-immunity between these diseases, and pertussis vaccination does not protect against parapertussis.

The most frequent symptom (85% of cases) was paroxysmal cough and the second most frequent (70%) vomiting. The symptoms of respiratory tract infection were often so severe that antibiotic therapy had been instituted by the referring physician. Cyanosis had been present before admission in 25% of the children, preponderantly those under one year of age, but no correlation was found between the occurrence of cyanosis and the incidence of pneumonia. In patients over one year of age vomiting invariably accompanied cyanosis. Convulsions, otitis media, and diarrhoea were infrequent. Two types of complication directly related to treatment with tetracycline drugs were observed—4 patients developed staphylococcal enterocolitis and in 2 cases a severe laryngotracheitis was observed. Although the leucocyte count in pertussis is usually described as characteristically greater than 20,000 per c.mm., this was not the case in 43% of the present series. There was no relation between the leucocyte count and positive culture for *H. pertussis*. Of the 3 patients who died, all of whom were under one year of age, 2 had involvement of the central nervous system.

The results of this study indicate that the neonate can best be protected against pertussis by primary immunization or booster inoculation of siblings during the maternal gestation period. *R. G. Meyer*

1146. **The Clinical Picture of *Salmonella* Infection in Children.** (К вопросу о клинике салмонеллезов у детей)
L. V. Poljak. *Педиатрия* [*Pediatrija*] **38**, 3–7, April, 1960. 5 refs.

The clinical features of 77 cases of salmonellosis in children, of whom 24 were less than one, 19 between one and 2, 23 between 2 and 7, and 11 over 7 years of age, are analysed. In 67 cases salmonellae of Group B were discovered (*Salmonella breslau*, 44; *Salm. reading*, 17; and *Salm. heidelberg*, 6). In the other 10 cases the organisms were of Groups C, D, and E. Salmonellae were found during the first week of the illness in half of the cases, while in the others they were detected during the second week or (in Group-B cases only) later. In the author's experience the *Salmonella* infection can be detected during the first week in almost 60% of cases, a fact which is important for the differential diagnosis of bacillary dysentery from other gastro-intestinal diseases.

The main symptom was colitis in 41 cases, dyspepsia in 10, and enteritis in 6, while in 3 cases the illness took a typhoid form. In 38 cases the illness was acute (2 of these being described in detail), in 15 subacute, and in 7 chronic. In all cases there was a moderate leucopenia, but the erythrocyte sedimentation rate was not affected. In 40% there was a definite nuclear deviation and lymphopenia. Agglutination reactions were performed in 30 cases, in half of which there was a positive reaction with killed suspensions in dilutions of 1:200 to 1:1,600, while in all cases the reaction with live cultures was positive in dilutions of 1:400 to 1:3,200. The author stresses the great importance of differential diagnosis by means of thorough bacteriological and serological examinations. *H. W. Swann*

1147. **The Syndrome of *Toxoplasma* Epilepsy.** (О токсоплазмозном эпилептиформном синдроме)
A. M. Halecki. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 307–311, No. 3, 1960. 8 refs.

The commonest precursory signs of congenital toxoplasmosis are chorio-retinitis, delayed psychophysical development, epileptiform convulsions, hydrocephalus, macrocephaly, and calcification in the brain. The author doubts the reliability of the Sabin–Feldman dye test, the complement-fixation test, and the skin-allergy reaction of Frenkel because they are often positive in healthy children. The acquired form of the disease is even harder to diagnose.

He reports observations on 9 children with an epileptiform syndrome, 8 of whom had congenital and one acquired toxoplasmosis. Of these, 2 were twin sons of a mother who was found to have a strong complement-fixation reaction for toxoplasmosis and had ailed since childhood with intermittent pyrexia, vertigo, and headaches. Both children were idiots and had chorio-retinitis. Two other children were the son and daughter of a woman who had toxoplasmosis, but who had previously given birth to 3 healthy sons, so that her disease was regarded as acquired. The boy, an idiot who had cried day and night without ceasing since birth and had convulsions and high pyrexia, gave a negative response to the Sabin–Feldman test, but the girl and the mother gave positive responses. In 7 of the congenital cases marked chorio-retinitis was present.

Pyrimethamine in combination with a sulphonamide was effective in ameliorating the symptoms and especially in increasing the efficacy of anticonvulsants, which had previously failed to control the attacks. One characteristic of the attacks in this disease is that they occur in series accompanied by high pyrexia and are specially prone to do so during intercurrent infections. The dosage of pyrimethamine employed was 25 to 50 mg. daily for 10 days and of the sulphonamide 2 to 3 g. daily. The general mental state was unaffected, as was the ultimate progress of the disease. Most of the children were apparently normal at birth, the convulsions beginning a few months to 2 years after birth, often after some slight infection. *L. Firman-Edwards*

Tuberculosis

1148. **The Supplementary Treatment of Tuberculosis in Infants and Young Children with Corticosteroids.** (Über die ergänzende Behandlung der Säuglings- und Kleinkindertuberkulose mit Corticosteroiden)
H. KRUKOWSKA. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **121**, 523–534, 1960. 7 figs., 8 refs.

In the Children's Department of the Tuberculosis Research Institute in Warsaw 50 children were treated with various corticosteroids in addition to isoniazid plus streptomycin or PAS in tuberculous infection. Sixteen of the patients were infants and all 50 were considered to be seriously ill on admission.

Three children with pleural effusion and 14 with either coarse or fine disseminated pulmonary lesions responded very well to treatment, and the speed of their response is attributed to the adjuvant effect of the steroids. Of the children with miliary shadows, there were 3 who had associated caseous pneumonia with cavities. One made a good recovery; the second improved greatly, though there is residual cavitary tuberculosis of lobar distribution for which lobectomy is planned; the third made good progress, but after some months contracted an influenza-like illness and died, caseous pneumonia being still present at necropsy.

The response of the 33 children with primary tuberculosis, which was judged by their clinical progress and the changes in the radiological picture and in the bronchoscopic appearances, was not nearly so uniformly favourable. Only 15 showed undoubted improvement; in 12 it was doubtful and in 6 it was not noticeable. In 4 children fresh radiological shadows appeared after initial improvement. Lesions of long standing responded least satisfactorily. On bronchoscopy swelling of the bronchial mucous membrane was seen to regress, though relapse was common if steroid treatment was of short duration. Endobronchial granulations were seen in 11 children; these disappeared in 6 cases, diminished in size in 3, and remained unaltered in 2. In one child granulations appeared for the first time during treatment. The influence of corticosteroids on the general condition of children with primary tuberculosis was not impressive, and 9 of the 33 developed bronchiectasis later.

In conclusion the author feels that corticosteroids in association with chemotherapy may be life-saving in very ill children with miliary tuberculosis and are generally useful in all forms of childhood tuberculosis if given early in the course of the disease. Treatment should be given for 1 to 2 months in moderate dosage to avoid side-effects.

[Similar results can be achieved without steroids in most cases of disseminated tuberculosis and pleural effusion, and in primary tuberculosis even without chemotherapy. That steroids occasionally have life-saving properties in initially severely toxic cases, however, is probably true.] *John Lorber*

1149. **Emergence of Streptomycin-resistant *Mycobacterium tuberculosis* in Infected Animals not Subjected to Streptomycin Therapy.** (Об образовании у туберкулезных микобактерий резистентности к стрептомицину в организме инфицированных животных, не подвергавшихся стрептомицинотерапии)
K. K. MEDNE. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Ž. Mikrobiol. (Mosk.)*] **31**, 45–49, May, 1960. 12 refs.

This investigation was undertaken in an attempt to explain some of the mechanisms underlying the emergence of streptomycin-resistant tubercle bacilli *in vivo*. Five groups of 10 guinea-pigs each were infected with 1 million organisms of a standard bovine strain of *Mycobacterium tuberculosis* (Walle). The sensitivity of this strain to streptomycin was 15 μg. per ml. One group of guinea-pigs served as controls, while the other 4 groups were exposed to additional stresses, such as daily subcutaneous injections of distilled water from the 1st day of infection onwards or from the 20th day of infection onwards and a vitamin-C-deficient diet with and without daily injections of distilled water. After intervals varying up to 4 months the guinea-pigs were killed and the infecting strain of tubercle bacillus isolated from the site of infection, the regional lymph nodes, and the internal organs. The sensitivity to streptomycin of the strains thus isolated was then tested.

Strains isolated from the control group were 3·3 to 6·6 times more resistant to streptomycin than the original infecting strain. Strains from the group of guinea-pigs injected with distilled water from the 20th day onwards were 6·6 to 33 times more resistant, those from animals injected with distilled water from the 1st day onwards were 1 to 66 times more resistant, those from the group fed on a vitamin-C-deficient diet 33 to 66 times more resistant, and those from guinea-pigs exposed to the double stress of both vitamin-C deficiency and daily injections of distilled water were 33 to 330 times more resistant than the original strain. [These results were not subjected to statistical analysis.]

On the basis of these findings it is thought that not all streptomycin-resistant strains of *M. tuberculosis* isolated from patients arise as a consequence of streptomycin treatment either of the same patient or of a contact, but that a proportion arise as a result of some stress mechanism operating in man. *K. Zinnemann*

1150. **Tuberculosis of the Middle Ear**
A. L. JEANES and I. FRIEDMANN. *Tubercle* [*Tubercle (Lond.)*] **41**, 109–116, April, 1960. 5 figs., 10 refs.

Between 1950 and 1959 tuberculosis of the middle ear was diagnosed in 12 patients at the Royal National Throat, Nose and Ear Hospital, London. The ages of the patients (9 male and 3 female) ranged from 2 to 74 years, 7 being under 20 years of age. The infection in

5 patients appeared to be confined to the ear, but in 7 there were signs of tuberculosis elsewhere. The presenting signs and symptoms were those of acute otitis media in 5 cases and of chronic and painless otorrhoea in 7. All the patients were deaf, the deafness usually being severe and persistent. In 2 cases there were two perforations of the tympanic membrane, a condition which is considered to be pathognomonic of this type of infection. The authors state that clinical diagnosis is difficult in the absence of evidence of other forms of tuberculosis, and they suggest that when otitis media does not respond readily to ordinary treatment the aural discharge should be examined for the presence of *Mycobacterium tuberculosis*. The value of routine histological examination of material removed at operation for middle-ear infection is emphasized. All the patients were subjected to mastoid surgery, which was usually followed by a course of antituberculous drugs. *Arthur Willcox*

1151. **Tuberculous Meningitis since the Introduction of Isoniazid**

A. PINES. *Tubercle* [*Tubercle* (*Lond.*)] **41**, 117–122, April, 1960. 11 refs.

Experience in the treatment of 39 cases of tuberculous meningitis seen in the Department of Tuberculosis and Diseases of the Respiratory System, University of Edinburgh, between 1953 and 1958 is reported. Of the 39 patients, 26 of whom were under 10 years of age, 15 were fully conscious and 4 were unconscious on admission; the remainder had various degrees of disturbed consciousness. Choroidal tubercles were seen in 11 patients on admission. In 26 cases streptomycin was given intrathecally in addition to systemic isoniazid, PAS, and streptomycin; intrathecal injections were not given in the remaining 13. In this respect the two groups were not comparable; most of the late cases were given intrathecal therapy. There were 7 deaths, 6 in the group given intrathecal injections and one in the group treated systemically, an over-all mortality of 18%. The average duration of treatment was 15 months in those who had had intrathecal injections [number not stated], and 21 months in those not given intrathecal injections. [This is a considerable difference in favour of the cases given streptomycin intrathecally, especially since they were the more severe.] One survivor, who developed diabetes insipidus, is well maintained on vasopressin. One child aged 17 months became grossly retarded, deaf, and blind, and another also became grossly retarded. There are no detectable sequelae in 26 of the 32 survivors. *John Lorber*

1152. **Treatment of Tuberculous Meningitis**

J. LORBER. *British Medical Journal* [*Brit. med. J.*] **1**, 1309–1312, April 30, 1960. 2 figs., 7 refs.

Since 1947, 210 children suffering from tuberculous meningitis have been treated at Sheffield Children's Hospital. Streptomycin alone was given before 1950 to 82 children; 30 of these survived and 20 of them did not develop neurological sequelae. During the following 3 years 48 children received PAS in addition to streptomycin and 35 recovered, 30 without nervous sequelae. Since 1952 80 children have received streptomycin, PAS and isoniazid; 66 survived and 55 had no neurological sequelae. Adjuvant methods of treatment such as intrathecal tuberculin, intrathecal cortisone, and oral cortisone were given to some of these patients. Although the number of intrathecal injections of streptomycin has been considerably reduced, the author does not advocate abandoning such intrathecal therapy altogether. A detailed therapeutic regimen is described. The results of treatment are less favourable in children under the age of 3 years and also when the tuberculous disease is advanced before treatment is started. *R. M. Todd*

RESPIRATORY TUBERCULOSIS

1153. **Antimicrobial–Steroid Treatment of Active Pulmonary Tuberculosis as a Routine Measure**

H. MARCUS and P. CHRISTOPOULOS. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **105**, 542–559, April, 1960. 10 figs., 26 refs.

Prednisone or prednisolone in varying dosages together with different combinations of antimicrobial drugs was tried in the routine treatment of pulmonary tuberculosis at the Bronx Municipal Hospital Center and Grasslands Hospital, Valhalla, New York, the results in 30 cases so treated being compared with those in 30 cases given isoniazid, streptomycin, and sometimes also PAS, but no steroids. There was greater and more accelerated improvement in the steroid-treated group than in the controls. The improvement was most marked in the early months of treatment, but was still discernible at the end of the observation period of 3 months. Of the 30 patients given prednisolone, 24 showed moderate, marked, or very marked radiological improvement at the end of 4 weeks, while in the control group improvement was seen in only 2 patients. Eventually 27 patients in the steroid group showed clearing compared with 11 patients in the control group. Complications which developed in 3 patients given prednisolone were thrombophlebitis of the leg in one, non-pitting supraclavicular swellings in another, and gastro-intestinal haemorrhage and diabetic coma, which proved fatal, in the third. *G. M. Little*

1154. **Pulmonary Tuberculosis Treated with High Doses of INH plus Glutamic Acid**

F. O. SEGARRA and D. S. SHERMAN. *Diseases of the Chest* [*Dis. Chest*] **37**, 382–389, April, 1960. 1 fig., 14 refs.

The effect of high doses of isoniazid with and without glutamic acid in the treatment of pulmonary tuberculosis was studied at the Boston Sanatorium, Massachusetts, in 14 male patients aged 23 to 69 years. All the patients had far-advanced disease and had received 600 mg. of isoniazid daily for a period of 6 months. Of the 14 patients, 9 served as controls and were given 20 mg. of isoniazid per kg. body weight daily with streptomycin and PAS, but not glutamic acid. The remaining 5 patients received 20 mg. of isoniazid per kg. daily and 10 mg. of monosodium glutamate for each mg. of

isoniazid. The authors state that "glutazide" was used, each capsule of which contained 50 mg. of isoniazid and 500 mg. of monosodium glutamate. Later in the trial 5 of the patients from the control group were given glutazide. All the patients received 100 mg. of pyridoxine daily, and the duration of treatment ranged from 3 to 10 months.

It was found that the toxicity of isoniazid was reduced by the simultaneous administration of glutamic acid, this finding being confirmed by the results of liver function tests and by serial electroencephalograms. In all the patients given glutamic acid there was a markedly increased appetite, with gain in weight and a sense of well-being. Euphoria was noticeably increased. The authors were unable to come to any conclusions concerning the effect of this treatment on the disease. Except in one case, none of the chest radiographs could be considered to show any improvement. Only 7 patients had a positive sputum before the start of the trial and only in 3 cases were the organisms still sensitive to isoniazid, the others being resistant; in none of the cases did the sputum become negative during treatment with high doses of isoniazid. *Kenneth M. A. Perry*

1155. **Comparative Trial of Isoniazid Alone in Low and High Dosage and Isoniazid plus PAS in the Treatment of Acute Pulmonary Tuberculosis in East Africans**

A Co-operative Investigation in East African Hospitals and Laboratories with the Collaboration of the British Medical Research Council. *Tubercle* [*Tubercle* (*Lond.*)] **41**, 83–102, April, 1960. 32 refs.

The investigations reported here were carried out in 8 hospitals in Africa (one in Uganda, 2 in Kenya, and 3 in Tanganyika) and in laboratories in Nairobi and Dar-es-Salaam, with the cooperation of various centres and research groups in London. The reasons for making the trial were as follows. (1) Isoniazid is easily administered and cheap, and is therefore considered by a number of authorities to be the best treatment for large numbers of out-patients with pulmonary tuberculosis in primitive communities. (2) Indeed isoniazid alone is already being used in many areas, and it is important to discover if this is wise. Such treatment is certainly sometimes followed by great clinical and radiological improvement. (3) A significant number of patients after treatment with isoniazid alone may remain sputum-positive, the tubercle bacillus being resistant to isoniazid. However, the importance of these organisms to the patients and their contacts is unknown.

[The article itself should be consulted for the account in detail of the conduct of the trial and its results. The authors' summary, which appears below, gives a lucid account of what was achieved.]

"One hundred and twelve East Africans with acute bilateral pulmonary tuberculosis, with organisms initially sensitive to isoniazid and to PAS, were treated in hospital for one year, either with isoniazid alone in low dosage 200 mg. daily (40 H patients), or with isoniazid in high dosage 20 mg. per kg. body weight daily plus pyridoxine 5 mg. per kg. (37 HIP patients), or with isoniazid 200 mg. daily plus PAS (sodium salt) 10 g. daily (35 10PH patients), the treatment for each patient being allocated at random. The three series were reasonably similar initially in most respects, although the H series had fewer patients with extensive initial cavitation.

"There were no toxic reactions in the H series. In the HIP series one patient had a hypersensitive reaction, one showed mental confusion and 2 had transient peripheral neuritis (one also with subsequent mental confusion). In the 10PH series one patient had a very severe hypersensitive reaction. There were 3 deaths in each of the H and the HIP series and 2 in the 10PH series. Chemotherapy was changed because of radiographic or clinical deterioration in 5 of the H, 6 of the HIP and none of the 10PH patients. All three series showed substantial clinical and radiographic progress; on average the patients in the H series progressed least well, and those in the 10PH series improved most.

"The bacteriological differences between the series were similar but greater. At the end of 6 months, negative culture results were obtained in 39% of the H, 50% of the HIP and 87% of the 10PH series; the corresponding figures at 12 months were 57% of the H, 67% of the HIP, and 84% of the 10PH series. The positive cultures in the H series were heavier than those in the HIP series which in turn were heavier than those in the 10PH series. An assessment based on all the culture results during treatment showed that at the end of the year 61% of the H, 54% of the HIP and 19% of the 10PH series had bacteriologically active disease. All the positive cultures from all three series at 6, 9 and 12 months contained isoniazid-resistant strains. At 12 months, isoniazid-resistant strains were found in 53% of the H, 33% of the HIP, and 19% of the 10PH patients. PAS-resistant strains were present in 4 of 5 cultures from the 10PH patients at 12 months.

"A substantial proportion of the patients originally allocated treatment in the trial were found to have had organisms initially resistant to isoniazid, or PAS, or both, and were consequently excluded from the main analysis. However, a special study was made of these patients, a number of whom continued on the allocated chemotherapy for 12 months. Treatment with isoniazid alone in patients presenting with isoniazid-resistant strains was much less effective radiographically and bacteriologically than in those with initially sensitive strains.

"In terms of mass chemotherapy for severe, extensive disease in Africans, isoniazid alone in low dosage is inadequate, and if this drug is to be used alone, a higher dosage is indicated. It is not possible to indicate, however, what the higher dosage should be, because of possible interference with the effect of the isoniazid by the high dosage of pyridoxine employed. Isoniazid plus PAS was more effective than either regimen containing isoniazid alone, and should be recommended in preference, at present, for patients with severe disease."

Arthur Willcox

1156. **Bronchography in Pulmonary Tuberculosis**

N. C. Elphinstone and S. Z. Kalinowski. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **54**, 277–282, July, 1960. 14 refs.

Venereal Diseases

1157. **Is Trichomonal Infestation a Venereal Disease?**
R. D. CATTERALL and C. S. NICOL. *British Medical Journal* [*Brit. med. J.*] **1**, 1177–1179, April 16, 1960. 18 refs.

An investigation was carried out among patients attending the venereal disease departments of the London Hospital and St. Thomas's and St. Bartholomew's Hospitals, London, to determine whether infection due to *Trichomonas vaginalis* is venereally transmitted. The female sexual partners of 56 males with *T. vaginalis* urethritis were found to have *T. vaginalis* vaginitis. Of the 56 females, 5 stated that they were virgins until they had intercourse with their present partners and that vaginitis appeared from 5 to 28 days after the first intercourse.

The authors suggest that these findings support the view that *T. vaginalis* infections are usually venereally transmitted. Patients with *T. vaginalis* infections should be referred to venereal disease clinics so that sexual contacts can be traced, examined, and treated if they are found to be infected. Sexual intercourse should not take place until the parasite has been eradicated from the genital tract of both partners. Such measures might lead to improvements in the unsatisfactory results at present obtained with various forms of treatment.

G. W. Csonka

1158. **Fluorescent Treponemal Antibody Test. Modification Based on Quantitation (FTA-200)**
W. E. DEACON, E. M. FREEMAN, and A. HARRIS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol.* (*N.Y.*)] **103**, 827–829, April, 1960. 5 refs.

The fluorescent treponemal antibody (F.T.A.) test described by Deacon *et al.* (*Proc. Soc. exp. Biol.* (*N.Y.*), 1957, **96**, 477; *Abstr. Wld Med.*, 1958, **24**, 26) was shown to have a high specificity and sensitivity in an evaluation of serological tests for syphilis carried out by the U.S. Public Health Service in 1956–7. The introduction of fluorescein *iso*thiocyanate for labelling anti-human globulin sera and the incorporation of " tween 80 " to enhance antigen–antibody coupling were thought to have increased the sensitivity of the test at the expense of specificity; because of this, some modifications in technique have been introduced.

It is now recommended that sera should be tested at a dilution of 1:200 instead of 1:5. Results are expressed as reactive or non-reactive, and sera producing weak (1+) fluorescence are to be classed as non-reactive. Four out of 25 sera from patients presumed to be non-syphilitic gave 1+ fluorescence at a dilution of 1:100, but all were negative at the chosen critical dilution of 1:200. Tests on sera from patients in whom the diagnosis of syphilis was established showed that 8 out of 10 from cases of untreated primary syphilis were reactive, as were all of 4 cases of treated primary, 10 of untreated secondary, 5 of treated secondary, and 28 of treated late syphilis. Quantitative tests showed that the titres ranged up to 1:25,600. In these small numbers of cases the F.T.A. test appeared to be more sensitive than the T.P.I., Reiter protein complement-fixation, and V.D.R.L. slide tests. Duplicate testing of dilutions of pooled positive sera in two different laboratories showed that the revised technique (which the authors call the F.T.A.–200 method) gave good reproducibility. Unpublished work is said to suggest that the low-grade (1+) fluorescence found with some presumed non-syphilitic sera is probably due to treponemal antibodies not associated with syphilis.

[It seems that this test, although potentially of great importance, must still be regarded as an experimental procedure and is not yet acceptable for adoption in practice.] *A. E. Wilkinson*

1159. **Nonspecific Immobilization in the *Treponema pallidum* Immobilization (TPI) Test**
R. W. SANDERS, D. R. PIPER, W. A. HOOK, and L. H. MUSCHEL. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **33**, 135–137, Feb., 1960. 4 refs.

The presence of toxic substances in the serum may result in immobilization of treponemes in the treponemal immobilization (T.P.I.) test with inactivated complement. The causes of such non-specific immobilization may be drugs or toxic agents developed in transit. An attempt is reported from the Walter Reed Institute of Research, Washington, D.C., to overcome this difficulty by obtaining the euglobulin fraction of the serum by precipitation with hydrochloric acid, redissolving the precipitate in saline, and testing this fraction for the presence of T.P.I. antibodies. Of 148 sera which had given non-specific results in the standard T.P.I. test, 117 gave a satisfactory result when the euglobulin fraction was used, while 31 sera behaved as before.

Determinations on non-toxic sera indicated that restoration of the euglobulin solution to one-half of the original volume of serum resulted in a comparable concentration of immobilizing antibody as in the original serum, indicating that approximately one-half of the immobilizing antibody is contained in the euglobulin fraction of the serum. *R. R. Willcox*

1160. **The Reiter Protein Complement Fixation Test as a Diagnostic Aid in Syphilis**
W. G. SIMPSON, A. HARRIS, W. GARSON, and W. L. BUNCH JR. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **81**, 904–907, June, 1960. 3 figs., 2 refs.

Tropical Medicine

1161. **The Pathogenesis of Anaemia in Kwashiorkor.** [In English]
KHO LIEN-KENG and W. A. F. J. TUMBELAKA. *Annales paediatrici* [*Ann. paediat.* (*Basel*)] **194**, 257–272, May, 1960. 6 figs., 41 refs.

A clinical and haematological study of 150 cases of kwashiorkor seen during the past 5 years at the Paediatric Clinic of the University of Indonesia, Djakarta, is presented. The authors divide the types of anaemia present into four groups as follows. (1) Hypoplastic or aplastic anaemia which was resistant to treatment, characterized by a high myeloid:erythroid ratio and a great decrease in number both of erythroblasts in the bone marrow and of reticulocytes in the peripheral blood. (2) Hypochromic anaemia probably due to simple iron deficiency. (3) Megaloblastic anaemia, which, in the classic form, was rare. However, the authors suggest that the frequent finding of giant stab cells in marrow films indicates that a deficiency of folic acid was probably often present. (4) Active normoblastic anaemia which did not react to iron or folic acid treatment.

The authors emphasize that the erythropoietic system in children with malnutrition is very labile, aplastic crises being frequently observed. They attribute the poor response to the usual haematopoietic remedies that was observed in many cases to general metabolic disturbances associated with malnutrition. *Janet Vaughan*

1162. **The Free Aminoacids of Plasma and Urine in Kwashiorkor**
J. C. EDOZIEN, E. J. PHILLIPS, and W. R. F. COLLIS. *Lancet* [*Lancet*] **1**, 615–618, March 19, 1960. 3 figs., 27 refs.

The authors report the results of an investigation by paper chromatography of the free amino-acids in the plasma and urine in 50 untreated cases of kwashiorkor admitted to the University College Hospital, Ibadan, Nigeria. For a few hours after admission the children, aged 1 to 4 years, were kept on glucose and water with added potassium until fasting blood and urine samples could be taken. Thereafter 41 of them were treated with a high-protein milk diet, while the remaining 9, who were not so severely ill, received a diet high in carbohydrate and low in protein for 4 days, at the end of which time further samples were taken and the child given the high-protein milk diet; of this group of 9 children, 6 received an additional supplement of 2 g. of methionine per day while taking the high-carbohydrate diet. A group of 25 healthy children of the same race and age served as controls.

The mean fasting value for plasma amino-acid nitrogen in the kwashiorkor patients was only 45% of normal. In the chromatograms the amino-acids most affected were cystine, methionine plus valine plus tryptophan (as one spot), leucine plus phenylalanine (one spot), threonine, and arginine. Ethanolamine was present in 75% of the patients, but in none of the controls, while β-amino-*iso*butyric acid was also present in 30% of the patients but not in the controls. The urinary excretion of amino-acids in the controls was similar to that in healthy European children, ethanolamine being absent in all cases and β-amino*iso*butyric acid present in only 8%. Every patient with kwashiorkor, however, excreted β-amino-*iso*butyric acid and 80% excreted ethanolamine. Treatment with a high-carbohydrate, low-protein diet did not alter the urinary chromatogram, but did reduce the intensity of the spots in the plasma chromatogram. Supplementation of the diet with methionine produced a marked increase in levels of all plasma amino-acids, and in the 3 cases in which ethanolamine was present it disappeared. Methionine supplementation also caused a great decrease in the excretion of ethanolamine in all 6 such cases, but it did not affect the excretion of β-amino-*iso*butyric acid.

The authors conclude that in kwashiorkor there appears to be a decrease in the renal threshold for amino-acids. The greatly increased excretion of β-amino*iso*butyric acid may be due either to increased breakdown of deoxyribonucleic acid or else to a block in the utilization of this amino-acid, while they consider that the accumulation of ethanolamine is due to a block in the utilization of this substance resulting from a deficiency of methyl donors. *W. H. Horner Andrews*

1163. **Humatin in Intestinal Amebiasis**
S. BELL and A. W. WOODRUFF. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **9**, 155–157, March, 1960. 2 refs.

"Humatin" (paromomycin) is an antibiotic isolated from a species of *Streptomyces*. At the Hospital for Tropical Diseases, London, the effect of paromomycin on intestinal amoebiasis was studied in 20 patients passing cysts of *Entamoeba histolytica* in the stools. The drug was given by mouth in a dosage of 30 mg. per kg. body weight daily for 10 days. Blood and urine were examined before and after treatment.

In 14 cases in which stools were examined daily during treatment the mean time of cyst clearance was 3·7 days. Of 19 patients followed up for periods ranging from one month to over a year, one relapsed. In one patient haemorrhagic lesions of the lower bowel were still present one week after completing treatment. Although no amoebae were found in the faeces or in scrapings from the lesions, the absence of healing suggested that infection deep in the bowel mucosa had not been eradicated. A course of emetine bismuth iodide resulted in complete resolution of the lesions. Examination of blood and urine disclosed no side-effects, but in 6 patients diarrhoea occurred which ceased soon after completion of treatment. *I. M. Rollo*

Nutrition and Metabolism

1164. **Effect of a Saturated Medium-chain Triglyceride on Serum-lipids in Man**

S. A. HASHIM, A. ARTEAGA, and T. B. VAN ITALLIE. *Lancet* [*Lancet*] **1**, 1105–1108, May 21, 1960. 2 figs., 12 refs.

Butter and coconut oil raise the serum cholesterol level in man, and it has been suggested that this may be due to the fact that these fats have a relatively high content of medium-chain saturated fatty acids. An investigation is reported from St. Luke's Hospital and the Institute of Nutrition Sciences, Columbia University, New York, in which the effect of a triglyceride fat containing only fatty acids with an even number of carbon atoms ranging from C_6 to C_{12} (M.C.T.) was compared with that of butter, which is known to raise the serum cholesterol level, and that of corn oil, which is known to lower it. The three fats were incorporated into a formula diet as the only source of fat, this diet being given to 8 patients in different sequences. When given after butter, M.C.T. caused a considerable fall in the serum cholesterol level, which rose again when butter was re-introduced. When given after corn oil there was at first a transient rise in the serum cholesterol level and then a slow fall to a level only slightly higher than that achieved with corn oil. This study seems to exclude the possibility that the cholesterol-raising properties of fats may be associated with their content of medium-chain saturated fatty acids.

R. Schneider

1165. **Leucine and Pellagra**

C. GOPALAN and S. G. SRIKANTIA. *Lancet* [*Lancet*] **1**, 954–957, April 30, 1960. 4 figs., 6 refs.

Struck by the discrepancy in the incidence of cases of pellagra in Coonoor (South India), where it is rare, and in Hyderabad, 500 miles to the north, where it is relatively frequent, the authors, working at the Nutrition Research Laboratories of the Indian Council of Medical Research, Hyderabad, examined the diet of the poor population in both districts. No striking differences were found with regard to the intake of different nutrients, but whereas the staple diet in Coonoor consisted of rice, in Hyderabad, it always included millet (jowar). In practically all cases of pellagra investigated by the authors in Hyderabad there was a history of regular consumption of jowar with or without rice. In only one case was maize consumed in addition to jowar and rice.

The nicotinic acid and tryptophan content of rice, jowar, and maize is approximately the same, but both maize and jowar contain 60 to 90% more leucine than rice. Daily administration of 5 g. of leucine to 2 healthy volunteers for a week raised the urinary excretion of N-methyl nicotinamide (N.M.N.) by about 50%. A similar increase in the urinary excretion of N.M.N. was observed in a pellagrous patient when the rice in the diet was replaced by an isocaloric and isonitrogenous amount of jowar. Administration of 5 g. of L-leucine daily to 4 patients with pellagra for a week had no appreciable effect on the clinical picture. When, however, 20 to 30 g. of L-leucine was given daily to 2 pellagrous patients not only did the N.M.N. excretion rise sharply, but their clinical condition also deteriorated immediately. Administration of nicotinic acid after the discontinuation of leucine was followed by immediate improvement.

The role of leucine in nicotinic acid metabolism and pellagra needs further investigation. The authors, however, cautiously suggest a possibility of amino-acid imbalance precipitated by the relative excess of leucine in patients living continuously on a protein-poor diet.

Z. A. Leitner

1166. **Diet and Weight-reduction in the Obese**

T. R. E. PILKINGTON, H. GAINSBOROUGH, V. M. ROSENOER, and M. CAREY. *Lancet* [*Lancet*] **1**, 856–858, April 16, 1960. 9 figs., 5 refs.

Kekwick and Pawan (*Lancet*, 1956, **2**, 155; *Abstr. Wld Med.*, 1957, **21**, 23) found that during short periods on isocaloric submaintenance diets weight loss was greater when most of the calories were supplied by fat than when most were supplied by carbohydrate. Since they had not observed failure to absorb fat or change in basal metabolic rate they suggested that this difference was due to a specific dynamic action of fat much larger than had previously been observed. Their findings have been used by others as a basis for slimming diets.

In an investigation carried out at St. George's Hospital, London, the experiments of Kekwick and Pawan were repeated on 9 obese patients and continued not for periods of a few days, but for periods of weeks and months. It was found that if the periods of study were long enough to achieve a "steady state" the rate of weight loss on a diet consisting mainly of fat did not differ significantly from the rate of weight loss on an isocaloric diet consisting mainly of carbohydrate. When these diets were interchanged deviations from the weight curve occurred, lasting up to 10 days; these could be accounted for mainly by changes in the fluid balance. As observed by Kekwick and Pawan, the changes occurred even when the salt content of the diets was kept constant.

A. G. Mullins

1167. **Fatty Foods and Obesity**

E. S. OLESEN and F. QUAADE. *Lancet* [*Lancet*] **1**, 1048–1051, May 14, 1960. 4 figs., 6 refs.

In recent years there has been a widespread popular belief that if the diet is sufficiently low in carbohydrate, the obese patient will lose weight even if the calorie intake considerably exceeds that of the composite diet on which he had previously remained overweight. At Kommunehospitalet, Copenhagen, experiments were carried out designed to show whether there is any basis for this belief. The authors point out that the theory is valid only if the fatty food is capable of augmenting energy expenditure.

The following diets were given to 8 obese women in hospital: (1) plain composite food *ad libitum* for 7 to 10 days; (2) a diet with a high fat content yielding 1,500 to 2,600 Calories and a carbohydrate content of 25 to 40 g. for 9 to 22 days; and (3) a diet of low calorie value (about 1,250) but of comparatively high carbohydrate content for 5 to 7 days. The authors' findings are as follows: (1) A high-fat, low-carbohydrate diet may reduce the weight of obese people considerably, but this weight loss ceases after a few days and may be explained largely, perhaps wholly, by loss of water. (2) Continued intake of a high-fat, low-carbohydrate diet affects body weight in the way expected from the number of calories ingested. (3) A stable body weight can be maintained on a diet containing a relatively high proportion of carbohydrate but with a calorie intake below the theoretical minimum. This may occur if the diet is taken after a period on a high-fat diet and is probably attributable to simultaneous increase of the fluid content of the body. (4) In a single experiment such a high-carbohydrate diet continued for 3 weeks produced a loss of weight which was identical with that produced during the next 3 weeks by an equicaloric high-fat diet. (5) The oxygen consumption of the obese patients, measured during rest and during standardized exertion, was no higher on a fatty diet than on an ordinary composite diet.

These findings do not lend support to the theory that weight can be lost on a high-fat, high-calorie diet. However, the authors point out that this study does not answer the question of whether a high proportion of fat makes it easier for obese patients to restrict their calorie intake. *A. G. Mullins*

1168. **Jejunal Biopsy in Adult Coeliac Disease and Allied Disorders**

D. J. Fone, W. T. Cooke, M. J. Meynell, D. B. Brewer, E. L. Harris, and E. V. Cox. *Lancet* [*Lancet*] **1**, 933–939, April 30, 1960. 3 figs., 39 refs.

At the General Hospital, Birmingham, jejunal mucosa obtained by peroral biopsy (mostly with the Crosby capsule) from 58 patients with " idiopathic steatorrhoea " diagnosed after full clinical, radiological, and laboratory investigation was examined and compared with specimens from 65 control subjects, either healthy or not suffering from idiopathic steatorrhoea. [The findings in this control group are not reported. The subjects included some patients with steatorrhoea from pancreatic disease, regional enteritis, and enterocolitis.]

An abnormal mucosa was found in 54 patients with idiopathic steatorrhoea. In 27 cases (Group I), there was marked atrophy of the mucosa, the surface being flattened, with absence or gross abnormality of the villi. There was a mild or moderate increase in cellularity of the lamina propria, mostly due to plasma cells. In 27 cases (Group II) the mucosa was also abnormal, but differed from that of Group I in that villi were always present, but were mostly abnormal, while the surface epithelium was not so flattened and the cellular infiltration consisted mostly of lymphocytes, histiocytes, and spindle cells, plasma cells usually being less evident. Second biopsies, obtained from 5 patients after an interval of at least a year, were not significantly different from the first biopsies.

The authors suggest that the patients in Group I form a homogeneous group on clinical grounds as well as in their mucosal pattern and that only cases of this type should be called adult coeliac disease. Patients in Group II fell into two categories, one with malaise and mild diarrhoea, the other with severe anaemia of relatively short duration. Some patients in both groups responded well to a gluten-free diet. The authors also suggest that many causes operate in Group II, some cases being due to a chronic jejunitis with various degrees of mucosal atrophy.

[Although the clear-cut separation on clinical and histological grounds of a homogeneous Group I may be correct, this division cannot be made with conviction from the data presented in this paper. The main difference between the groups appears to be the presence of a vitamin-B_{12}- or folic-acid-deficient anaemia in Group II. The occurrence of diarrhoea, malaise, weight loss, achlorhydria, steatorrhoea, an abnormal xylose excretion, abnormal folic acid excretion, and remission due to a gluten-free diet appears to have been similar in both groups.] *M. Lubran*

1169. **Clinical Assessment of Intestinal Fat-absorption Using Radioactive Fat**

W. F. Walker, W. K. Stewart, H. G. Morgan, and J. McKie. *British Medical Journal* [*Brit. med. J.*] **1**, 1403–1406, May 7, 1960. 5 figs., 24 refs.

In investigations reported from Queen's College, Dundee, olive oil labelled with about 25 μc. of ^{131}I was given, with 60 ml. of inactive olive oil, after an overnight fast, to 32 normal adults and to 6 patients with steatorrhoea. The subjects then ate a standard breakfast and later took their normal ward diet. Blood was taken after 2, 4, 6, and 9 hours and urine collected daily for 3 or 4 days. Six-day chemical fat balances were carried out on 4 patients with idiopathic steatorrhoea (absorption 24·3 to 87%) and one with post-gastrectomy steatorrhoea (absorption 68%). Faecal fat was not measured in the remaining case, one of obstructive jaundice.

Plasma levels of radioactivity were lower in the patients than in the normal subjects, but at all times there was an overlap between the two groups. There was no appreciable peak activity. Measurement of the activity in the urine on the other hand showed a clear-cut division between controls and patients for all 3 daily collections. In the first 24 hours the normal subjects excreted an average of 52% (S.D. 12·0) of the dose and the patients 10·4% (S.D. 4·9). No normal subject excreted less than 30% and no patient more than 20% of the dose in the first 24 hours. The authors suggest that an excretion of 25% of the dose or less indicates steatorrhoea.

[In view of the small number of patients examined, at least 5 of whom had a severe degree of steatorrhoea as judged by faecal fat measurements, and the failure of other authors studying larger series of patients to find a similar unequivocal correlation between steatorrhoea and urinary excretion, the views expressed by the authors should be accepted with reserve.] *M. Lubran*

Gastroenterology

1170. **Recurrent Mikulicz's Aphthae Treated with Topical Hydrocortisone Hemisuccinate Sodium: Double-blind Controlled Clinical Trial**

B. E. D. Cooke. *British Medical Journal* [*Brit. med. J.*] 1, 764–766, March 12, 1960. 4 figs., 2 refs.

Working at Guy's Hospital, London, the author has investigated the effects of oral tablets containing 2·5 mg. of hydrocortisone hemisuccinate with a lactose base on recurrent oral ulceration typical of Milkulicz's aphthae in 17 cases. The patients were instructed to take 4 tablets daily when ulcers were present and 2 daily when they were absent, the tablets being allowed to dissolve in the region of the ulcers. Each was given a period of hydrocortisone treatment and a comparable period of treatment with placebo tablets, neither the patient nor the investigator knowing the nature of the tablets in any given case at the time that the results were being assessed. The trial periods lasted 8 weeks, with an intervening period of 2 weeks without treatment. In one-half of the cases the placebo tablets preceded the hydrocortisone tablets and in the other half this order was reversed.

Two criteria were used to evaluate the results, the number of new ulcers that developed and the number of "ulcer days" in a given period—that is, the sum of the duration of all ulcers during that period. There was a significantly better response to the hydrocortisone than to the placebo tablets, both the mean number of new ulcers appearing and the mean number of ulcer days being about 50% less while hydrocortisone tablets were being taken than during the placebo period. Complete remission occurred in 4 cases, 3 with hydrocortisone and one with the placebo. After the trial period hydrocortisone tablets were prescribed in varying maintenance doses and with varying response. It did not appear that the treatment in any way induced a remission, and even the full dose of 4 tablets a day did not prevent exacerbations. Such complete remissions as occurred were thought to be the result of the natural history of the disease. Individual case histories are given to illustrate the different types of response. *T. D. Kellock*

1171. **An Effective Treatment of Refractory Ascites in Cirrhosis of the Liver**

A. G. Redeker, O. T. Kuzma, and T. B. Reynolds. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **105**, 594–600, April, 1960. 3 figs., 4 refs.

Refractory ascites in cirrhosis of the liver is not unusual, and radical measures such as portacaval shunt and bilateral adrenalectomy have been tried in attempts to control ascites formation. The authors of this paper from John Wesley County Hospital and the University of Southern California School of Medicine, Los Angeles, describe the results obtained with a combination of chlorothiazide and 6-methyl prednisolone in 18 cases of chronic and refractory alcoholic cirrhosis. In all the cases ascites had been present for periods of 2 months to 2 years and control had been attempted with a variety of measures. The drugs were given in a dosage of 2 g. of chlorothiazide and 12 to 16 mg. of 6-methyl prednisolone daily. The body weight, volume of urine, and the amounts of sodium and potassium excreted were recorded.

The results were excellent in 15 of the 18 patients. The average sodium excretion rose over a 24-hour period from 3 mEq. with chlorothiazide alone to a mean of 76 mEq. with chlorothiazide combined with prednisolone. This was accompanied by an average fall in body weight of 21 lb. (9·5 kg.) and a decrease in the ascites. Potassium excretion also increased in spite of supplementary potassium by mouth. No complications were noted. In the remaining 3 cases there was no response to this treatment. *John Fry*

1172. **The Serum Leucine Aminopeptidase Test: an Appraisal of Its Value in Diagnosis of Carcinoma of Pancreas**

J. Harkness, B. W. Roper, J. A. Durant, and H. Miller. *British Medical Journal* [*Brit. med. J.*] **1**, 1787–1790, June 11, 1960. 4 figs., 7 refs.

Results of 750 estimations of serum leucine aminopeptidase on 671 subjects do not support claims that a normal level would exclude the diagnosis of a carcinoma of the pancreas. In our hands the test did not distinguish between carcinoma of the pancreas and other causes of jaundice; it merely denoted the presence of an obstruction to the biliary flow, without reference to the cause of obstruction. Only extremely rarely does this test yield information not already supplied by the established tests of serum bilirubin and serum alkaline phosphatase.—[Authors' summary.]

1173. **Pancreozymin–Secretin Test: the Combined Study of Serum Enzymes and Duodenal Contents in the Diagnosis of Pancreatic Disease**

D. C. H. Sun and H. Shay. *Gastroenterology* [*Gastroenterology*] **38**, 570–581, April, 1960. 2 figs., 35 refs.

Pointing out the need for a reliable test for the diagnosis of chronic pancreatic disease the authors report, from Temple University Medical Center, Philadelphia, the preliminary results obtained with a provocative blood enzyme test which they devised for this purpose. The pancreatic stimulant used was pancreozymin followed after 10 minutes by secretin, both substances being given intravenously. The serum lipase and amylase levels were measured before and again at 1, 2, and 4 hours after the injections, and the duodenal contents were also analysed. The detailed results are tabulated and the methods fully described. The test was performed on 52 patients, of whom 25 (controls) showed no evidence of gastro-intestinal disease and 27 had

disease of the pancreas. In the control group the serum levels of amylase and lipase after pancreozymin–secretin stimulation in no case rose above the upper limit of normal. The duodenal contents were analysed for 18 of the control patients so as to determine the lower limit of normal values (calculated as the mean value less twice the standard deviation); for total volume and maximum bicarbonate concentration only the 60-minute post-secretin time was considered, but for amylase content the 70-minute post-pancreozymin value was taken, since more than one-third of the total amylase output occurs in the first 10 minutes.

The pancreozymin–secretin test gave a positive serum enzyme response (that is, a rise in level above the upper limit of normal) in 9 of the 18 patients with chronic pancreatitis, the serum amylase level being raised in 3, the lipase level in 5, and the level of both enzymes in one; it is therefore recommended that the level of both enzymes should be estimated. Of these 9 patients, 5 had normal duodenal contents. On the other hand all the patients with a negative serum enzyme response had one or more abnormally low values in the duodenal studies. All the 3 patients with carcinoma of the ampulla of Vater showed a positive serum enzyme response, but only one out of 5 patients with carcinoma of the pancreas did so and all of the latter also had low duodenal values. One case in which acute monocytic leukaemia was infiltrating the pancreas showed very low serum amylase levels and also low values in the duodenal contents.

The authors discuss their results, correlating the serum enzyme response with the underlying pathology in the pancreas. They recommend that " in cases of suspected pancreatic disease, the provocative serum enzyme test with pancreozymin and secretin be done first; if negative to be followed by a duodenal intubation study". They suggest that because of its relative simplicity the provocative serum enzyme test could be included in the routine investigation of chronic pancreatic disease.

I. Berkinshaw-Smith

1174. **Fulminating Ulcerative Colitis: Recent Experience in Management**

J. E. Lennard-Jones and A. B. Vivian. *British Medical Journal* [*Brit. med. J.*] **2**, 96–102, July 9, 1960. 2 figs., 14 refs.

The authors have studied 32 patients with severe acute ulcerative colitis treated at St. Mark's and the Central Middlesex Hospitals, London, between 1951 and 1959, during which period a total of 520 cases of all types of ulcerative colitis were admitted. An exact definition of fulminating colitis was not found to be possible. Operation was performed on 16 patients at the height of their illness, and histological examination of the resected portion of the colon revealed grossly dilated vessels and separation of muscle fibres by oedema; the ulcers were large and deep and, in 13 cases, had spread to the muscle coat, while in 10 cases the serosa was also involved; in all 16, however, the terminal ileum was normal, and the caecum was intact in 10. In only 6 cases was the whole colon involved.

Of the 7 patients given steroid therapy (up to 120 units of ACTH daily), 3 recovered without surgery; even larger doses of ACTH may be desirable. Of the 8 treated with steroids and also surgically, 4 died and only 2 made an uncomplicated recovery. But 2 of the patients who died underwent operation not covered by steroids and the operation was unjustifiably delayed, while a further patient possibly died also because of delay in operating. Although all 4 patients who were initially subjected to ileostomy (with colectomy later) recovered, whereas 3 who underwent primary colectomy died and another 4 had a complicated recovery, the authors nevertheless consider that these figures were the result of chance and they recommend primary colectomy whenever possible. In conclusion they point out that no less than one-third of these patients died of their illness and that only 4 of 31 were treated successfully by medical means alone. In a proposed regimen of management they suggest that when remission cannot be induced by steroids then energetic correction of protein, water, and electrolyte depletion and early operation are essential, but the dangers of perforation of the bowel during its handling must be borne in mind. In addition, the patient's emotional troubles must be dealt with adequately. In their experience the broad-spectrum antibiotics appear to be of little value.

A. Gordon Beckett

1175. **Acute Fulminating Ulcerative Colitis with Colonic Distention**

G. W. Peskin and A. V. O. Davis. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **110**, 269–276, March, 1960. 5 figs., 14 refs.

The authors review the condition of fulminating ulcerative colitis, the problem of its diagnosis, and the rationale of its treatment. They give details of 9 cases treated at the Hospital of the University of Pennsylvania, Philadelphia.

All the patients were young, their average age being just under 30. In nearly all cases the total history of the disease was short and in all the duration of the acute phase was less than 3 weeks. Six of the patients had had treatment with cortisone without benefit. There was well-marked distension of the colon on clinical and x-ray examination and in 7 of the 9 the colon had already perforated at the time of operation, which was performed in all cases. Six patients underwent immediate subtotal or total colectomy with ileostomy. One patient, who was pregnant, underwent transverse colostomy and remains well nearly 3 years later. One patient who was initially treated by ileostomy alone did so poorly that colectomy was necessary within one month and another patient treated by colostomy for decompression and ileostomy required colectomy 2 years later.

There were no immediate deaths after the primary operation. One patient died 3 months later after intestinal haemorrhage and abscess formation, one treated initially by ileostomy alone died of septicaemia 3 days after colectomy one month later, and a third patient died after an abdomino-perineal resection of the rectum 2½ years after the primary operation.

The authors conclude that ileostomy with simultaneous colectomy is the correct treatment for this type of case.

T. D. Kellock

Cardiovascular System

1176. **The Clinical Use of Polybrene as an Antiheparin Agent in Open Heart Surgery**
J. B. BLUMBERG, L. C. WINTERSCHEID, D. H. DILLARD, R. R. VETTO, and K. A. MERENDINO. *Journal of Thoracic and Cardiovascular Surgery* [*J. thorac. cardiovasc. Surg.*] **39**, 330–336, March, 1960. 7 refs.

Heparin is usually given to prevent blood clotting during open heart operations with extracorporeal circulation. At the end of the perfusion the heparin must be neutralized in order to re-establish the normal clotting mechanism. Until recently protamine was generally used for this purpose, and although usually effective it has the following disadvantages: it is unstable; accurate calculation of the dosage is necessary, since it may occasionally show paradoxical activity; it may cause a marked fall in the blood pressure; its action is not instantaneous; and lastly its potency varies.

The authors report from the University of Washington School of Medicine, Seattle, that they now use " polybrene " and, in the 47 cases in which it has been used so far, have found it superior to protamine. Polybrene is a stable quaternary ammonium salt which causes a rapid conversion to a normal clotting time. Although itself an anticoagulant there is a wide margin between its antiheparin and its anticoagulant dosage. Its advantages are that its potency is uniform, and it does not cause hypotensive reactions, though too rapid injection may cause dizziness. It may, however, be antigenic, so is best avoided in patients with allergy. They usually employ it in a dosage equal to that of heparin, mg. for mg., and give it slowly intravenously. About one patient in 10 requires a supplementary dose. Of the 47 patients so treated, 2 developed transient urticaria and one died from generalized bleeding which was attributed to an unexplained haemorrhagic diathesis not related to the use of polybrene. *M. Meredith Brown*

1177. **A Review of Four Dreaded Complications of Open-heart Operations: Causes, Avoidance, and Treatment of Acidosis, Overoxygenation, Heart-block, and Pulmonary Damage**
W. J. KOLFF, D. B. EFFLER, and L. K. GROVES. *British Medical Journal* [*Brit. med. J.*] **1**, 1149–1153, April 16, 1960. 1 fig., 24 refs.

Clinical observations on 150 consecutive patients who underwent open-heart operations were corroborated by laboratory experiments. The conclusions derived were later confirmed in the open-heart operations in 330 consecutive patients.

1. Acidosis is most severe three or more hours after operation. It may be expected not only after open-heart operations but also after other operations, whenever a low cardiac output as evidenced by low blood-pressure has been present for a considerable time. The younger the patient the more likely it is to occur. Acidosis mainly occurs when there has been trouble, and, if severe, may lead to death unless it is controlled by intravenous infusion of sodium bicarbonate.

2. Overoxygenation does not occur in nature, and it is unlikely that the human organism has a defence mechanism against it, though it has not been proved to have a deleterious effect.

3. Heart-block can occur after operations in the neighbourhood of the A-V bundle. It is no longer justifiable to undertake an open-heart operation without a pacemaker at hand. Whenever heart-block occurs, one electrode is sewn to the myocardium before the chest is closed, even though the heart-rate while the patient is on the operating table is still satisfactory.

4. Pulmonary complications in open-heart operations can nearly always be avoided. The most important single measure to prevent pulmonary complications is the use of a wide cannula in the left atrium, to measure the pressure in the left atrium, and to drain out blood into the pump oxygenator if this pressure proves to be too high. Pulmonary damage during open-heart operations is usually due to temporary overfilling of the pulmonary vascular bed with blood, leading to capillary damage. The conditions under which this may occur can be predicted. Dynamic insufficiency of the left ventricle is perhaps the most frequent cause. Increased bronchial flow in tetralogies and open ductus are other causes.—[Authors' summary.]

1178. **Familial Muscular Subaortic Stenosis: an Unrecognized Form of " Idiopathic Heart Disease ", with Clinical and Autopsy Observations**
L. B. BRENT, A. ABURANO, D. L. FISHER, T. J. MORAN, J. D. MYERS, and W. J. TAYLOR. *Circulation* [*Circulation*] **21**, 167–180, Feb., 1960. 13 figs., 27 refs.

The authors of this paper from Allegheny General Hospital and the University of Pittsburgh School of Medicine, Pittsburgh, describe the clinical and necropsy findings in a series of patients with muscular subaortic stenosis, which, they consider, is a hitherto unrecognized form of idiopathic heart disease. The patients belonged to two families and the occurrence of the disease in three generations suggests that the defect is related to Mendelian dominant inheritance. The aetiology is unknown. Familial muscular subaortic stenosis is caused by a marked localized hypertrophy in the interventricular septum at the outflow tract which gives rise to an obstruction during systolic contraction. Necropsy findings include a healthy aortic valve, hypertrophy of the entire left ventricle, and almost complete obliteration of the left ventricular cavity by the greatly hypertrophied muscle mass, considerable resistance being encountered when the finger is forced into the left ventricle. The obstruction lies 1 to 2·5 cm. below the base of the aortic valve. Histologically, there is slight endocardial thickening over

the subaortic region and moderate hypertrophy of the muscle fibres. Differential diagnosis from other types of aortic stenosis appears possible and is of some importance because the familial muscular type is not suitable for surgery. Syncope and severe anginal pain are frequent symptoms and sudden death is common.

A. I. Suchett-Kaye

1179. **Effect of Oxygen Therapy on Oedema in Patients with Cor Pulmonale**

P. Effersöe, H. S. Kristensen, and H. C. A. Lassen. *British Medical Journal* [*Brit. med. J.*] **1**, 1469–1473, May 14, 1960. 4 figs., 14 refs.

The authors of this paper from Blegdam Hospital and the University of Copenhagen describe 3 cases of decompensated cor pulmonale in which oedema was reduced by oxygen therapy—spontaneous respiration with oxygen administration in 2 cases and artificial ventilation in a tank respirator with oxygen administration in one. Although all other measures designed to reduce oedema had been ineffective, a remission and diuresis were obtained in all 3 cases.

It is considered that the improvement was due in part to improved tissue oxygenation. During tank respiration there was also diminished consumption of oxygen by the tissues because respiration was aided mechanically, and pressure variations in the thorax probably increased the urinary output through the medium of pressure-sensitive receptors in the thorax. *J. B. Wilson*

1180. **Serum Transaminase in Endomyocardial Fibrosis**

J. Campbell and K. Somers. *British Medical Journal* [*Brit. med. J.*] **1**, 1540–1541, May 21, 1960. 1 fig., 12 refs.

In the light of our present experience we do not consider estimation of serum transaminase a diagnostic aid in established endomyocardial fibrosis. In the clinical syndromes of endomyocardial fibrosis the serum transaminase levels are usually within the normal range. The reasons for this are discussed. Serum transaminase may have diagnostic value in an " acute phase " of endomyocardial fibrosis, but such a lesion has yet to be recognized.—[Authors' summary.]

1181. **Subacute Bacterial Endocarditis**

D. W. Barritt and W. A. Gillespie. *British Medical Journal* [*Brit. med. J.*] **1**, 1235–1239, April 23, 1960. 13 refs.

A retrospective study of the records of all cases of subacute bacterial endocarditis seen at the United Bristol Hospitals between 1950 and 1958 in which blood cultures had been obtained revealed 60 cases (67 attacks) of bacteriologically confirmed subacute bacterial endocarditis, a positive culture being obtained from the first specimen in 63 of the 67 attacks. Of 60 other cases in which bacterial endocarditis was suspected (but in 56 of which no antibiotics were given) the clinical progress excluded the disease in all but 4 cases; of these 4 patients, 2 showed no valvular vegetations post mortem and alternative diagnoses were confirmed at necropsy on the remaining 2. Treatment was with large doses of penicillin, and of the 62 patients who left hospital, 57 (85%) survived for one year or more.

A considerable number of the blood cultures were obtained while the patient was afebrile, and the authors see no point in delaying the administration of antibiotics, provided three cultures have been taken and set up for aerobic and anaerobic organisms. In the whole series over the 8½ years only 5 possible examples of subacute bacterial endocarditis with persistently negative blood cultures were found and these cases are described in detail; the authors suggest that the finding of a persistently negative blood culture in this disease is less common than has been hitherto supposed. Previously reported similar series are briefly reviewed.

J. Robertson Sinton

CONGENITAL HEART DISEASE

1182. **The Use of Phenylephrine in the Differentiation of Fallot's Tetralogy from Pulmonary Stenosis with Intact Ventricular Septum**

L. Vogelpoel, V. Schrire, M. Nellen, and A. Swanepoel. *American Heart Journal* [*Amer. Heart J.*] **59**, 489–505, April, 1960. 5 figs., 8 refs.

In this study, reported from the University and Groote Schuur Hospital, Cape Town, the diagnostic value of phenylephrine in the differentiation of Fallot's tetralogy from pulmonary stenosis with intact ventricular septum was investigated by noting the effects of the drug on the systemic and right ventricular pressures in 9 cases of the tetralogy and 5 of pulmonary stenosis during cardiac catheterization; in one case of each of the conditions the effects on the blood pressure and phonocardiogram were studied after intravenous injection of the drug. After control measurements had been made 0·25 mg. of phenylephrine was injected through the cardiac catheter into the right ventricle and the right ventricular and systemic pressures recorded either immediately consecutively or (in more recent cases) synchronously. A pressor response was usually noticeable about 15 seconds after injection of the drug, but if this response was slight another 0·25 mg. was given. The phonocardiogram was recorded continuously at slow paper speed (2·5 to 8 mm. per second), with frequent recordings at fast paper speed (80 mm. per second) during held expiration. Samples of arterial blood were taken before and during the peak action of the drug in several cyanosed patients. Amyl nitrite was administered in most cases, being given several minutes after the injection of phenylephrine while the pressures were subsiding but still high. These abrupt changes in the systemic resistance brought about by the consecutive use of the two drugs provided valuable information about the state of the ventricular septum in difficult cases.

In the cases of Fallot's tetralogy, whether the patient was severely cyanosed or acyanotic, the systemic and right ventricular systolic pressures rose and fell together and could not be separated. Since the rise in systemic pressure was transmitted to the right ventricle there was an increase in the pressure gradient across the stenosis, causing an increased intensity and length of the murmur

and intensification of the closure sound of the pulmonary valve. These changes were rendered more obvious by the bradycardia induced by the phenylephrine. In the cyanosed patients there was a rise in the arterial oxygen saturation. Amyl nitrite abruptly reversed these effects by lowering the systemic arterial resistance. In contrast, in the cases of pulmonary valvular stenosis, whether mild or severe, the systemic and right ventricular pressures behaved independently. As there was no significant change in right ventricular pressure, so there was no significant change in the murmur. In patients who developed marked systemic hypertension the left ventricular systole appeared to be delayed, so that the second sound became less widely split.

That the difference in response between Fallot's tetralogy and pulmonary stenosis was due to the presence or absence of a ventricular septal defect was proved by the results in one case of the tetralogy which was studied before and after complete repair of the septal defect. The authors conclude that their observations support the thesis that in Fallot's tetralogy the pulmonary blood flow and hence the length and intensity of the murmur are determined by both the systemic resistance and the severity of the stenosis, and that phenylephrine is a useful means of determining whether or not the ventricular septum is open in cases of pulmonary stenosis, and possibly in helping to select the correct operative procedure in severe cases of the tetralogy.

Celia Oakley

1183. **Differentiation of Interatrial Communications by Clinical Methods. Ostium Secundum, Ostium Primum, Common Atrium, and Total Anomalous Pulmonary Venous Connection**

J. W. DuShane, W. H. Weidman, R. O. Brandenburg, and J. W. Kirklin. *Circulation* [*Circulation*] **21**, 363–371, March, 1960. 7 figs., 6 refs.

The clinical features important in the differentiation of the four types of interatrial communication were studied at the Mayo Clinic in 128 children with proven congenital heart disease. Of these patients, 74 had an ostium secundum, 37 an ostium primum, 12 total anomalous pulmonary venous connexion, and 5 a common atrium. Assessment was made on the history, clinical examination, and the findings on radiography, electrocardiography (including vector analysis), and cardiac catheterization (in 93 cases).

Symptoms were minimal in the patients with ostium secundum and primum, but recurrent respiratory infections, cyanosis, and even cardiac failure were frequent in those with a common atrium and anomalous drainage. A pulmonary systolic murmur, with or without a thrill, was audible in all 4 groups, while a wide, fixed, split P2 was present in three groups, but absent in those with anomalous drainage. An additional apical systolic murmur was frequent in the patients with ostium primum and a common atrium, and an additional diastolic murmur at the xiphoid area or apex was present often in those with ostium secundum and less frequently in the 5 with a common atrium. Radiologically, cardiomegaly and pulmonary engorgement were present in all groups, but a distinctive supracardiac shadow [" cottage-loaf "] was present in the group with anomalous pulmonary venous drainage. Vectorcardiograms were helpful, showing clockwise rotation of the QRS loop in the frontal plane with the major portion below the isoelectric line in ostium secundum and anomalous drainage and counter-clockwise rotation with the loop mainly superior to the isoelectric line in ostium primum and common atrium. In addition an incomplete pattern of right bundle-branch block occurred in ostium secundum and evidence of left ventricular overloading in ostium primum and common atrium. Cardiac catheterization showed similar findings of a left-to-right shunt at atrial level in the cases of ostium secundum and primum, but in common atrium and anomalous drainage there was evidence of a common mixing chamber and the oxygen saturation in the pulmonary artery was equal to or slightly higher than that in the systemic arteries.

Of the 128 cases, only 6 were not accurately diagnosed and the authors conclude that accurate differentiation, which is of practical importance in the selection of patients for surgical treatment, can usually be made by means of a careful medical history and clinical examination combined with radiology, electrocardiography, and catheterization. Finally it is pointed out that surgical repair of the defect performed in 124 out of the 128 patients resulted in only 7 deaths. *Gerald Sandler*

VALVULAR DISEASE

1184. **The Course of Mitral Stenosis without Surgery: Ten- and Twenty-year Perspectives**

J. C. Rowe, E. F. Bland, H. B. Sprague, and P. D. White. *Annals of Internal Medicine* [*Ann. intern. Med.*] **52**, 741–749, April, 1960. 3 figs., 4 refs.

The course of medically treated mitral stenosis was studied at the Massachusetts General Hospital and the Home of the Good Samaritan, Boston, in 250 patients who were followed up for a minimum of 10 years or until death, 115 being followed up for 20 years. The initial examination revealed signs of pure mitral stenosis in 128, a soft apical systolic murmur in addition in 53, a soft aortic diastolic murmur in 52, and both murmurs in 17. Four standard grades of increasing severity of the condition were recognized, and the patients (194 female and 56 male) were classed accordingly: Grade 1, 130 (52%); Grade 2, 92 (37%); Grade 3, 25 (10%); and Grade 4, 3 (1%). Only 33 patients were 50 and over; 83 were under 20 years of age.

Of the entire series, 61% lived 10 years. After 10 years two-fifths had died and one-fifth had deteriorated in grade. The cause of death was known in 110 cases: progressive heart failure, sometimes complicated by pulmonary embolism in 67; arterial embolism in 21 (19 women); subacute bacterial endocarditis (before the antibiotic era) in 5; and unrelated disease in 7.

The major symptoms and complications noted were as follows: (1) Dyspnoea had occurred in half of the patients when first seen and developed in two-thirds during the 10 years; fibrillation increased the dyspnoea. Acute pulmonary oedema was associated with advanced

disease or with unusual effort or pregnancy. (2) Atrial fibrillation was established in one-fifth of the patients when first seen (another 9% had paroxysmal fibrillation and 1% atrial tachycardia) and developed in one-third after 10 years. (3) Arterial embolism had occurred in 6% of all patients before the first examination and in 16% by the end of the tenth year, usually in those with atrial fibrillation. (4) Bacterial endocarditis was present in one patient when first seen and developed in 4 others during the 10 years (one having atrial fibrillation). (5) Hypertension (blood pressure over 170/100 mm. Hg) was noted in 6% of the series, the percentage remaining constant and the sex incidence equal during the 10 years.

Of the 115 patients followed up for 20 years—mostly older patients with more severe disease—43% had originally been classified Grade 1, 45% Grade 2, and 12% Grade 3 (compared with the percentages in these grades of the original 250 patients of 52, 37, and 10 respectively). After 20 years there was no change in grade of severity in 13% of these patients. Pulmonary oedema and congestive failure occurred more frequently in the patients observed for 20 years, and at the end of this period arterial embolism had occurred in 30 (26%).

From a composite curve of their results and those of other published series the authors found a 10-year survival of a little over 50% in 759 medically treated patients. *R. S. Stevens*

1185. **Effects of Atrial Fibrillation upon the Circulation in Patients with Mitral Stenosis**

A. SELZER. *American Heart Journal* [*Amer. Heart J.*] **59**, 518–526, April, 1960. 3 figs., 12 refs.

In a study of the effect of atrial fibrillation on the performance of the heart in mitral stenosis, here reported from the Veterans Administration Hospital (Stanford University School of Medicine), San Francisco, an attempt was made to evaluate the haemodynamic consequences of the presence or absence of this arrythmia when this was the only variable factor. Of the 67 patients with pure or dominant mitral stenosis investigated, 48 were in sinus rhythm and 19 had atrial fibrillation. The severity of the stenosis was judged by calculating the mitral valve area from data obtained at right heart catheterization, cardiac output being measured by the Fick principle. All the patients were in a stable state, without evidence of cardiac failure; in those with fibrillation the cardiac rate was controlled by digitalis.

Three patients were studied twice, once when in normal rhythm and once when in atrial fibrillation, but in 2 of these cases factors other than the type of rhythm might have varied between the studies, which were widely separated in time. However, all 3 patients showed a lower resting cardiac output during atrial fibrillation than during sinus rhythm. One patient showed no rise in cardiac output on effort during fibrillation, but a satisfactory rise when in sinus rhythm. (However, the latter study preceded that made during fibrillation by 3 years). An analysis of the findings in 15 pairs of these patients who were matched for severity of the mitral stenosis, age, and heart rate (so that the only difference between them was that one of each pair was in sinus rhythm and the other in atrial fibrillation) showed that the more advanced circulatory abnormalities present in the patients with fibrillation were related to the more frequent occurrence of fibrillation in patients with the more severe stenosis. However, for a comparable degree of stenosis 12 of the 15 patients in fibrillation showed a significantly lower cardiac output than those in sinus rhythm (average difference 0·37 litre per minute per sq. m.), and when measurements were made during exercise the average rise in cardiac output was significantly smaller in those with atrial fibrillation (average difference 0·54 litre per minute per sq. m.). The pulmonary arterial wedge pressure was also significantly lower (by 3·67 mm. Hg) in those with fibrillation, but these patients showed no significant difference between the pulmonary artery pressure at rest and that on effort.

It is concluded that in mitral stenosis atrial fibrillation results in a 20% fall in cardiac output both at rest and on exercise. The lower pressure in the left atrium in patients with fibrillation is a direct consequence of the lowered cardiac output, since for equally stenosed mitral valves the left atrial pressure is directly proportional to the flow through the valve. A 20% lowering of cardiac output following the onset of atrial fibrillation may make a considerable difference to the degree of disability in patients with mitral stenosis. *Celia Oakley*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1186. **Prevalence and Incidence of Coronary Heart Disease in Strata of the Labor Force of a Chicago Industrial Corporation**

J. STAMLER, H. A. LINDBERG, D. M. BERKSON, A. SHAFFER, W. MILLER, and A. POINDEXTER. *Journal of Chronic Diseases* [*J. chron. Dis.*] **11**, 405–420, April, 1960. 13 figs., 24 refs.

The data analysed in this report from the Medical Research Institute, Michael Reese Hospital, Chicago, were drawn from the medical and personnel records maintained by a Chicago public utility company whose middle-aged employees have been medically examined annually for some years. Although the scheme is voluntary, "base-line" data are available for 756 of the total of 784 male employees who were aged 50 to 59 in January, 1954, while follow-up data for the period 1954–7 are available for 740 of these men. The annual examinations numbered 627 in 1954, 599 in 1955, 652 in 1956, and 670 in 1957, as many as 433 men being examined in every one of these years and 604 in 3 of the 4 years. The examination included an interim medical history, physical examination, urine analysis, the recording of a 9-lead electrocardiogram, and a 35×42-cm. (14×17-inch) chest radiograph. Many of the men had worked for the company for many years (79% for 20 years or more) and sociological and medical data for earlier years could be studied when required. The authors define their clinical and diagnostic criteria in detail and describe their methods of handling the records.

Of the 756 men aged 50 to 59 in 1954, 19·4% had a diastolic blood pressure at that time of 95 mm. Hg or higher and in 14·6% it was between 90 and 94 mm. Hg. These groups are described as having hypertension and borderline diastolic hypertension respectively. Of the same total number, 21·6% were considered to be obese and 34·1% moderately obese. Also at the onset of the study 7% of the 756 men had coronary heart disease, 7% hypertensive heart disease, and about 13% other cardiovascular or renal disease. Incidence rates are defined as the " rates of development of new clinical disease in the population free of definitive signs of that disease at the beginning of the study ". The rates, expressed per 1,000 of the population for 4 years, for cardiovascular and renal diseases were: coronary heart disease 61, hypertensive heart disease 43, peripheral vascular disease 25, congestive heart failure 23, diabetes mellitus 15, cerebrovascular diseases 11, nephritis 9, and other heart disease 4. The rates for coronary heart disease for various population groups were: non-obese males 43, moderately obese 66, and markedly obese 87; normotensive 35, borderline hypertensive 97, and hypertensive 96; non-obese normotensive 28, and obese hypertensive 101. Of the 54 men with definite coronary heart disease at the beginning of the study, 7 died within the 4 years, giving a death rate of 130 per 1,000 in 4 years, compared with 28 per 1,000 in a group of 36 men with suspected coronary heart disease in 1954 and with 17 per 1,000 for all the other men. There were 19 deaths due to coronary heart disease among the 756 men, 8 of these deaths being sudden and in 5 cases the first manifestation of the disease. A table shows the other causes of death in the series.

The 756 men were classified into sub-groups according to a series of " sociological " factors, including place of birth (native-born or foreign-born), place of residence, military experience, education, occupation, physical activity at work, indoor or outdoor work, and amount of income. Diagrams for each sub-group show the prevalence of obesity and hypertension in January, 1954, and the incidence rates for coronary heart disease in the 4 years 1954–7. The authors conclude that the prevalence of hypertension and obesity was similar in the various sub-groups. Some of the diagrams relating to obesity suggest interesting trends, but apparently the differences between sub-groups could easily have arisen by chance. However, significantly higher incidence rates for coronary heart disease were observed in 431 native-born workers than in 236 foreign-born, the rates per 1,000 in the 4 years being 74 and 34 respectively.

E. A. Cheeseman

1187. Mortality from Coronary Heart Disease and Physical Activity of Work in California

L. Breslow and P. Buell. *Journal of Chronic Diseases* [*J. chron. Dis.*] **11**, 421–440, April, 1960.

It is noted that the excess mortality from coronary heart disease in men of the higher social classes reported for England and Wales has not been confirmed by various studies in different cities of the U.S.A. To throw further light on this discrepancy the authors present from the California State Department of Public Health a long and detailed analysis of the mortality attributed to arteriosclerotic heart disease " so described " and heart disease " specified as involving the coronary arteries " in males aged 20 to 64 years in California during the period 1949–51. [The methods of analysis closely follow those used by the Registrar-General for England and Wales and the authors conscientiously draw attention to the assumptions and imperfections inherent in the use of data of this kind.] They present standardized mortality ratios (S.M.R.) and mortality ratios for specific age groups for both a " social class " distribution and a " physical activity " distribution of occupations.

From the analysis by social class it is concluded that although mortality from all causes of death shows a fairly regular gradient (from low mortality in the highest social classes to high mortality in the lowest), there is no such gradient for arteriosclerotic disease, although for coronary heart disease there is a slight gradient in the opposite direction (from high mortality in Social Class 1 to low mortality in Social Class 5) among men aged 45 to 60 years. In regard to physical activity no consistent association was observed between physical activity at work and mortality from arteriosclerotic disease, but mortality from coronary heart disease in men aged 45 to 59 showed a regular trend compatible with a slight decrease in mortality as physical activity increased. In both diagnostic groups farmers and farm labourers at all ages had lower mortality rates than other men classified as doing " heavy " work.

Further analysis of the data for men in age group 45 to 64 was carried out by re-classifying the occupations into three " general mortality risk " groups based on the S.M.R. for all causes of death other than the cardiovascular diseases under examination. The effect of physical activity and social class on mortality from heart disease was then examined within each general mortality risk group. This analysis showed that when the general mortality risk was constant the following conclusions were true of mortality from both arteriosclerotic heart disease and coronary heart disease: (1) mortality in the lowest two social classes combined was always less than that in the higher social classes, and usually the highest two social classes had the highest mortality rates; (2) generally the mortality was lowest among men in work requiring most physical activity. When physical activity was held constant the mortality from heart disease of both types appeared to be highest in the group with high general mortality risk and lowest in that with low general mortality risk. Finally the authors attempt a threefold classification of the mortality, that is, by general mortality risk, social class, and physical activity, but for this purpose the number of deaths is said to be too small, particularly those from arteriosclerotic heart disease.

The authors make many comparisons with work done in England and Wales on this subject and conclude that " a gradient of decreasing mortality rates from coronary heart disease with increasing physical activity of work in middle-aged men, reported from England, is confirmed under special conditions in California data for 1949 to 1951. The California gradient is clearly revealed only in contrasts between occupational groups of similar

general mortality risk. The evidence for a social class gradient of coronary mortality in California is revealed in the same way, although it too is readily apparent in British studies without controlling general mortality risk. Earlier studies in the United States, which failed to confirm British results, have not included an analysis of general mortality. The apparently greater risk of coronary mortality in sedentary workers compared to heavy workers is of moderate degree, about 40% for occupations at average general mortality risk in the California data. Factors which increase the general mortality risk, and which had obscured the physical activity association, seem to account for as much coronary mortality as that possibly attributed to a limitation of physical activity in work."

(In a most useful appendix the authors set out the observed and expected numbers of deaths, used in calculation of the standardized mortality ratios, for specific occupations classified by the three factors, general mortality risk, social class, and physical activity.)

E. A. Cheeseman

1188. **A Study of the Pre-morbid Functional Condition of the Central Nervous System in Patients with Coronary Atherosclerosis and Angina Pectoris.** (О преморбидном функциональном состоянии центральной нервной системы у больных коронарным атеросклерозом с явлениями грудной жабы)

B. V. Il'inskij. *Терапевтический Архив* [*Ter. Arh.*] **32**, 3–8, April, 1960. 4 refs.

The author reports that a study of the pre-morbid history of 136 patients suffering from coronary atherosclerosis with angina pectoris revealed definite signs of neuropathy or neurosis in 91 cases. In 35 cases the anginal attacks were preceded by such disorders as arterial hypertension, tuberculosis, menopausal neurosis, and chronic toxic conditions usually associated with disorders of the higher nervous system. In 4 cases the anginal attacks followed immediately on severe psychological stress, while in a further 3 cases there was a long-standing history of strenuous work and insufficient sleep. In only 3 cases was there nothing unusual in the patient's antecedent history. All the 136 patients had been taking a diet rich in fat and cholesterol for a considerable length of time. With the development of the anginal attacks the functional nervous disturbances became worse.

A. Orley

1189. **Iproniazid in Treatment of Angina of Effort**

R. Fife, G. Howitt, and J. Stevenson. *British Medical Journal* [*Brit. med. J.*] **1**, 692–694, March 5, 1960. 9 refs.

Since the early reports of the dramatic relief of angina achieved with iproniazid (" marsilid ") enthusiasm for this drug has waned, further evidence having been conflicting and serious side-effects having been observed. In the double-blind trial of iproniazid in 51 patients with typical angina here reported from Glasgow Royal Infirmary (and which was begun before the toxicity of the drug had become apparent) the patients received iproniazid (50 mg. three times daily) and inert control tablets, each for 3 weeks, the frequency of attacks of pain, number of pain-free days, and side-effects in each period being compared, except that the first week of each of the two periods was discounted.

Iproniazid showed no significant effect; thus 14 patients considered iproniazid to be better than the control tablets, 12 preferred the placebo, 12 improved with both types of tablet, and 13 noted no change with either. Iproniazid appeared, however, to be of value in the 16 patients with severe angina, of whom 7 judged iproniazid to give better relief and only 2 preferred the placebo (this result is just under the 5% level of statistical significance). Side-effects of iproniazid were noted by 36 patients, especially dizziness, muscular weakness, and palpitations. Only 7 complained of side-effects while taking the control tablets. It is concluded that iproniazid may be of value in some patients with severe angina, but frequently causes undesirable side-effects.

David Phear

1190. **Evaluation of the Nitrites in the Treatment of Angina Pectoris**

H. I. Russek. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **239**, 478–486, April, 1960. 4 figs., 17 refs.

Previous observations have suggested that erythrol tetranitrate (ETN) and pentaerythritol tetranitrate (PETN) are effective in relieving the pain of angina pectoris when given sublingually, although when swallowed their effect may be slight. The author, working at the U.S. Public Health Service Hospital, Staten Island, New York, has found, however, that PETN is also effective when swallowed. He has now further investigated the clinical action of these drugs on 58 patients with typical angina pectoris who responded to both the prophylactic and therapeutic administration of nitroglycerin and all of whom had been under observation for more than a year; of these patients, 11 had previously suffered myocardial infarction. The tablet of the test drug or a matching placebo was administered sublingually or in the buccal pouch 3 times daily after meals in successive courses each of 2 weeks' duration. In 18 of the cases the electrocardiographic (ECG) response to standard exercise was recorded both while taking the placebo and while taking the drug. Measurements were also made of the degree of depression of the S–T segment observed in the post-exercise ECGs. Of the 58 patients originally included in the trial, 10 discontinued the drug treatment because of unpleasant side-effects.

While taking the placebo 36% of the patients, compared with 74% while taking ETN, reported " no pain " or " less pain " while under test. In 15 of 18 patients receiving ETN the drug exerted a marked modifying influence on the S–T-segment depression after exercise, the magnitude of the response being comparable to that following administration of nitroglycerin except that the duration of action was much longer, beginning about 5 minutes after the drug was inserted under the tongue and lasting for 1 to 2 hours. In 8 cases the effect of ETN given sublingually was compared with that of PETN given orally. The effects were similar, but with the latter drug they appeared only after an hour or more and lasted 4 to 5 hours. In contrast, PETN given sublingually

exerted only a relatively brief vasodilator effect immediately after its administration. In the prophylaxis of angina, therefore, PETN is far more effective when swallowed than when given sublingually, while the reverse is true of ETN. A serious drawback to the use of ETN sublingually is the frequency of headache (in 40% of cases), but this may disappear with increasing tolerance. PETN given orally rarely caused such a troublesome side-effect. The importance of the timing of the doses of PETN is stressed, it being pointed out that the therapeutic action of the drug is markedly diminished if it is taken after a meal. *R. Wyburn-Mason*

1191. **Myocardial Infarction in Patients Treated with Sippy and Other High-milk Diets: an Autopsy Study of Fifteen Hospitals in the U.S.A. and Great Britain**
R. D. Briggs, M. L. Rubenberg, R. M. O'Neal, W. A. Thomas, and W. S. Hartroft. *Circulation* [*Circulation*] **21**, 538–542, April, 1960. 1 fig., 10 refs.

This report, which is presented from Washington University, St. Louis, is based on material derived from 10 hospitals in the U.S.A. and 5 in Great Britain where the clinical and necropsy records for the years 1940 to 1959 were studied and all cases of chronic peptic ulcer collected. These were divided into two groups according to whether or not there was a history of treatment with a Sippy diet or its equivalent. (In the cases from Great Britain, where a Sippy diet is not commonly used, those patients with a history of increased intake of milk were placed in the Sippy diet group). Each ulcer patient was matched with a control subject by taking the record of the next necropsy performed on a patient with no ulcer but of the same age and race. Thus three groups were available for study with regard to the incidence of myocardial infarction.

In the American series there were 97 ulcer patients treated with a Sippy diet, 97 not so treated, and 194 non-ulcer patients, the corresponding figures for Great Britain being 95, 95, and 190. In the U.S. series 36% of ulcer patients given the Sippy diet had myocardial infarction compared with 15% of the non-Sippy-dieted ulcer patients and 15% of the non-ulcer patients. In the British series the corresponding figures were 18, 3, and 8%. It is suggested that the butter-fat content of the Sippy diet may be responsible for the differences in these results, but it is admitted that there is no definite proof of this. *C. Bruce Perry*

1192. **Serum-triglyceride Levels in South African Europeans and Bantu and in Ischaemic Heart-disease**
A. Antonis and I. Bersohn. *Lancet* [*Lancet*] **1**, 998–1002, May 7, 1960. 3 figs., 31 refs.

At the South African Institute for Medical Research, Johannesburg, the concentration and polyenoic-fatty-acid composition of the serum triglycerides was estimated in the blood of 46 male and 23 female healthy European subjects, in 57 healthy Bantu males, and in 23 European patients with ischaemic heart disease. It was shown that young European males, premenopausal European women, and Bantu males of all ages had a similar low serum triglyceride level. However, in European males over 40 years of age and in patients with ischaemic heart disease of various ages and both sexes the serum triglyceride levels were raised. It is suggested that it might be possible to predict which among older European males would be liable to develop ischaemic heart disease by determining the serum triglyceride level. *G. S. Crockett*

BLOOD VESSELS

1193. **Fibrinolysin (Plasmin) Therapy in Acute Deep Thrombophlebitis: a Controlled Study**
K. M. Moser, S. B. Sulavik, and G. C. Hajjar. *Circulation* [*Circulation*] **21**, 337–353, March, 1960. 1 fig., bibliography.

The value of a fibrinolytic agent used in conjunction with anticoagulant therapy was investigated in 32 out of 62 patients with acute deep venous thrombosis of varied aetiology in the lower limbs seen at the District of Columbia General Hospital (Georgetown University Medical School), Washington, D.C., the other 30 (alternate) patients serving as a control group. All patients were treated initially with bed rest, subcutaneous heparin, and a coumarin drug or warfarin; ambulation was allowed 2 days after subsidence of the acute phlebitic manifestations and the dosage of the anticoagulant drug then tapered off. Fibrinolysin was given in the trial group of 32 patients by intravenous infusion in a dose of "75 to 100,000 units" and repeated the next day, if phlebitic activity persisted, in a dose of "50 to 75,000 units". The clinical factors included in the assessment were time from onset of the phlebitis, duration of bed rest, amount of anticoagulant therapy, time required for subsidence of the acute inflammation, incidence of embolic and other complications, date of discharge, recurrence of phlebitis or embolization, and any residual changes in the lower limbs.

The results showed that combined fibrinolysin–anticoagulant therapy was followed by a more rapid resolution of the acute inflammatory process and a prompter return of the leg to normal size. Pulmonary embolism occurred during the first 2 weeks in 4 patients in the control group but in only one in the trial group, both having had a similar incidence of pulmonary embolism before treatment. No significant difference between the two groups was found in the incidence of post-phlebitic sequelae such as residual aching or oedema, and the difference in the recurrence rate of the phlebitis between the two groups was probably not significant, but the figures for each group were very small. Longer-term assessment, over 3 to 4 months, showed that late recurrence of phlebitis was frequent and not influenced by the type of initial treatment. The over-all mortality was higher in the control group than in the trial group; 4 of the 5 deaths in the former were attributed to embolism, whereas neither of the 2 deaths in the latter was due to this complication. Analysis of two subgroups in which treatment was instituted within 5 days of onset of the phlebitis accentuated the differences noted above, the more rapid resolution, the less frequent embolism, and the lower recurrence rate being all

more evident in the fibrinolysin-treated group, but again there was no significant difference in incidence of post-phlebitic sequelae.

The main toxic effect encountered with fibrinolysin was pyrexia, but the potential risk of anaphylactic reactions in allergic patients is pointed out. The authors conclude that fibrinolysin therapy together with anticoagulant therapy is promising in the acute stages of thrombophlebitis, but they are not prepared at present to draw any firm conclusions about the long-term results.

Gerald Sandler

1194. **Serum Lipoproteins in Patients with Intermittent Claudication and Myocardial Infarction**

P. J. NESTEL. *Circulation* [*Circulation*] **21**, 522–525, April, 1960. 1 fig., 18 refs.

The author describes a study which was carried out at the University of Melbourne on four groups of patients as follows: (1) 44 men, average age 61 years, with intermittent claudication (patients with diabetes mellitus, essential hypercholesterolaemia, or clinical evidence of a major arterial occlusion in the previous 6 months were excluded); (2) a control group of 61 men matched with Group 1 for age but with no symptoms; (3) 30 men, average age 49 years, who had had a myocardial infarction 3 to 4 weeks previously; and (4) 30 inmates of a home for elderly men who probably lacked exercise but who had no symptoms or signs referable to the cardiovascular system. The serum lipoproteins were separated by electrophoresis, stained with Sudan black B, and scanned. The ratio of β-lipoprotein to α-lipoprotein was the index measured.

In Group 1 the mean was 4·6, with a wide scatter of values; in Group 2 (controls) the mean ratio was 2·7, with a much narrower scatter; in group 3 the mean ratio was 3·1; and in Group 4 it was 2·9. Thus the only significant difference found was in Group 1, that is, the patients with intermittent claudication. Three possible reasons for this are discussed: (1) that this group probably had much more extensive arterial disease; (2) that many patients in this group had extensive thrombotic lesions in the legs and the high ratio might be associated with an increased tendency to thrombosis; or (3) that the incidence of atherosclerosis in different parts of the body may be governed by different factors.

C. Bruce Perry

1195. **Lipoproteins Quantitated by Paper Electrophoresis as an Index of Atherosclerosis**

M. WURM, R. KOSITCHEK, and R. STRAUS. *Circulation* [*Circulation*] **21**, 526–537, April, 1960. 13 figs., 44 refs.

This study was carried out at St. Joseph Hospital, Burbank, California, on 40 patients with evidence of one or more myocardial infarctions or arteriosclerotic cerebrovascular accidents and 40 individuals of comparable age with no evidence of cardiovascular disease who served as controls. Many of the patients in addition had other evidence of cardiovascular disease and 3 exhibited xanthomata with familial hypercholesterolaemia. In fasting blood specimens the serum cholesterol, lipid phosphorus, and total lipid content was estimated. The lipoproteins were separated by paper electrophoresis, stained, and scanned, and five fractions distinguished, namely, lipalbumin, α_1 lipoprotein, α_2 lipoprotein, β lipoprotein, and γ lipoprotein, as well as a neutral fat fraction. The β:α lipoprotein ratio was calculated by dividing the β-lipoprotein value by the combined values for α_1 and α_2 lipoprotein and lipalbumin. The β:lipalbumin ratio was also calculated. The values for serum cholesterol and phospholipid levels, their ratio, and serum total lipid content all had a very low order of significance in separating the atherosclerotic from the normal subjects. However, the values for lipalbumin and β lipoproteins and also the β:α lipoprotein and β:lipalbumin ratios showed a high level of significance in distinguishing normal from atherosclerotic individuals.

C. Bruce Perry

1196. **Arteriosclerosis Obliterans: Review of 520 Cases with Special Reference to Pathogenic and Prognostic Factors**

J. L. JUERGENS, N. W. BARKER, and E. A. HINES JR. *Circulation* [*Circulation*] **21**, 188–195, Feb., 1960. 1 fig., 3 refs.

The clinical and follow-up findings in a series of 520 patients in whom arteriosclerosis obliterans was diagnosed at the Mayo Clinic in the 10-year period 1939–48 are reviewed. The ratio of males to females was 11:1. The mean concentration of plasma cholesterol in men with arteriosclerosis obliterans was approximately 50 mg. per 100 ml. higher than in two control groups of men without clinical evidence of atherosclerosis. Only 2·5% of the male patients with arteriosclerosis obliterans were non-smokers. Obesity was not commonly associated with this condition, but hypertension was found in one-quarter of the patients, compared with only 9% of the controls. The survival rate in patients with arteriosclerosis obliterans was significantly lower than that in a normal population of a similar age and sex distribution, and in patients with coexistent coronary arterial disease the prognosis was poorer still. Patients with atherosclerotic aorto-iliac occlusion had a shorter expectation of life than those with occlusion of the femoral artery. Of the 520 patients, 4% required amputation of the leg soon after arteriosclerosis obliterans was diagnosed and an additional 4·9% required amputation during the 5-year period following the initial examination. No amputations were necessary among those smokers who abstained from smoking during the 5 years after the original diagnosis was made. *A. I. Suchett-Kaye*

1197. **Late Effects of Lumbar Sympathectomy on Blood-flow in the Foot in Obliterative Vascular Disease**

J. A. GILLESPIE. *Lancet* [*Lancet*] **1**, 891–894, April 23, 1960. 2 figs., 7 refs.

This paper contributes a useful long-term follow-up study of the effect of sympathectomy in 61 patients with obliterative vascular disease of the lower limb, the particular aspect studied being the blood flow through the foot, since the prime indication for sympathectomy today is an ischaemic foot in a limb not suitable for some form of direct arterial surgery. Of 100 consecutive patients subjected to lumbar sympathectomy between one

and 7 years previously for obliterative vascular disease, 25 had died before the investigation was initiated, 8 had had a major amputation of the affected limb, and 2 were untraced; of the remaining 65, 61 were fit and willing for blood-flow investigation. For comparison the blood flow was also measured in 18 patients who had undergone sympathectomy for non-obliterative disease during the same period.

The study showed that lumbar sympathectomy had produced a lasting doubling or trebling of the blood flow in the foot, and there was no evidence of this falling off with time during the period under review. The vasomotor test performed on 75 sympathectomized limbs showed that there was partial recovery of sympathetic vasomotor activity in 8 (11%), but this was always very incomplete. In the 20 cases in this series in which there had been ischaemic skin lesions of the foot these had healed after sympathectomy. The blood flow in these patients was significantly increased by the operation and was clearly a major factor in promoting healing. The author's conclusion is that measurements of blood flow in the foot provide objective physiological evidence " that lumbar sympathectomy is a good operation for promoting healing of existing ischaemic skin lesions and the lasting prevention of further ones ". *J. V. Crawford*

1198. **Vitamins A, E, and B_6 in the Treatment of Arteriosclerosis.** (Die Vitamine A+E+B_6 in der Behandlung der Arteriosklerose)
G. Schettler, K. Kirsch, E. Kuhn, M. Knedel, H. Ott, H. Schlüssel, P. Schölmerich, and W. Günther. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **85**, 732–740, April 22, 1960. 26 refs.

Following encouraging reports of experimental studies in animals, seven university clinics in Germany have collectively carried out a double-blind trial to test the effects of a combination of vitamins A, E (α-tocopherol), and B_6 (pyridoxine) on the symptoms and signs of arteriosclerosis, the subjects being 269 patients suffering from peripheral arteriosclerosis, coronary sclerosis, and so-called cerebral sclerosis; the duration of the trial was 12 months. Several combinations of the three vitamins were used and it is stated that improvement of subjective symptoms such as anginal pain, intermittent claudication, giddiness, and disturbances of memory and concentration were noted in a significantly higher proportion of the treated patients than of those receiving placebos. [The high percentage of patients (29%) who reported symptomatic improvement while taking the placebo is very striking, however, and must obviously reduce the significance of the previous observation.]

Objective tests such as serial electrocardiograms, two-step exercise tests, and measurement of the blood pressure and erythrocyte sedimentation rate showed no significant changes. Estimation of the plasma lipid levels (total lipids, cholesterol, neutral fats, and phospholipids) and electrophoretic analysis of lipoproteins and glycoproteins gave no consistent results. The authors therefore conclude that the trial produced no adequate evidence in favour of administration of vitamins A, E, and B_6 to patients suffering from arteriosclerosis.
A. J. Karlish

HYPERTENSION

1199. **Antihypertensive Drug versus Symptomatic Treatment in Primary Hypertension: Effect on Survival**
G. A. Perera. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **173**, 11–13, May 7, 1960. 5 refs.

Although antihypertensive drugs may prolong the life of patients in the accelerated phase of hypertension, their value in prolonging life in patients with early uncomplicated disease is less certain.

A study is reported from the Columbia University College of Physicians and Surgeons and the Presbyterian Hospital, New York, of the effect of these drugs in 29 pairs of hypertensive subjects (aged 41 to 52 years) matched for sex and all measured parameters. All had had established hypertension for at least 5 years before the trial, with at least one casually recorded standing diastolic blood pressure of 120 mm. Hg or higher. Other criteria for inclusion were absence of any evidence of antecedent myocardial infarction, retinal haemorrhages, or urea retention and no history of angina, congestive heart failure, or cerebrovascular accident. One of the matched groups received ganglionic blocking drugs, sometimes supplemented with *Rauwolfia* alkaloids and hydrallazine, and the other received sedatives such as phenobarbitone; both groups were given digitalis or diuretics when necessary. During the 7-year period of the study there were 16 deaths in each group; no significant difference in average survival was observed. Most of the deaths could be ascribed to atherosclerotic complications such as myocardial infarction or cerebrovascular accidents. *K. G. Lowe*

1200. **The Effect of Reserpine on the Coronary Circulation in Hypertension.** (Действие резерпина на коронарное кровообращение при гипертонической болезни)
S. K. Kiseleva. *Терапевтический Архив* [*Ter. Arh.*] **32**, 19–26, May, 1960. 3 figs., 29 refs.

The author reports a study of the effects of reserpine on the coronary arterial circulation in patients with hypertension. The doses of reserpine ranged from 0·1 to 0·25 mg., the average total daily dose being 0·6 mg., and the duration of the course of treatment from 15 to 60 days. The results, which were assessed clinically and also electrocardiographically, in 165 hypertensive patients so treated were compared with those in a similar group who were treated with spasmolytic drugs of the xanthine type.

A marked reduction in the hypertension was observed in 64% of the patients receiving reserpine and only in some 25% of those given the spasmolytic drugs. Reserpine also improved the adaptability of the coronary vessels to physical exertion to a much greater extent than did the spasmolytics. *A. Orley*

1201. **Chronic Pyelonephritis and Hypertension**
J. F. Gwynne. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **9**, 150–156, May, 1960. 8 figs., bibliography.

Clinical Haematology

1202. **Renal Polycythaemia**
N. F. JONES, R. W. PAYNE, R. D. HYDE, and T. L. M. PRICE. *Lancet* [*Lancet*] **1**, 299–303, Feb. 6, 1960. 2 figs., 27 refs.

Polycythaemia in association with renal carcinoma has been reported in over 30 cases and in association with other renal tumours, polycystic kidneys, or hydronephrosis in a few. The present authors describe 2 further cases of polycythaemia and non-neoplastic renal disease —unilateral hydronephrosis in one and unilateral polycystic kidney in the other. Neither thrombocytosis nor splenomegaly was present in either case, but leucocytosis was found in the second case. Nephrectomy was performed for the hydronephrosis and partial nephrectomy for the cystic kidney. In both cases after operation the polycythaemia disappeared and the total erythrocyte volume, the plasma iron turnover, and the plasma erythropoietin activity (measured by the reticulocytosis produced by intraperitoneal injection of plasma in rats) fell to normal levels. Blood samples taken at operation in the case of hydronephrosis showed higher erythropoietin activity in blood from a peripheral vein than in blood from the aorta or the renal vein of the affected side, which suggested that the abnormal kidney did not produce the erythropoietic factor, but influenced it indirectly.

The authors emphasize the importance of renal investigations and in particular of intravenous pyelography in all cases of polycythaemia, especially if leucocytosis, thrombocytosis, and splenomegaly are absent.

T. B. Begg

1203. **Polycythaemia Vera**
M. GARRETT. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] 224–236, May, 1960. 36 refs.

The treatment of polycythaemia vera with radioactive phosphorus (^{32}P) is of comparatively recent origin. This paper from the Radium Institute, Liverpool, describes the results of such treatment in 81 cases seen in the period 1944–57, this representing an average incidence of 3 per annum per million of the population served (2·05 millions), and compares the results with those in patients receiving initial x-ray therapy. The most frequent clinical manifestation was a plethoric appearance (97% of cases) and a "ruddy cyanosis" of the face, conjunctivae, tongue, and nail beds. Cerebral symptoms, pruritus, pain in the eyes and diplopia, and symptoms suggestive of peptic ulcer were also frequent. The haematological findings included an increased erythrocyte mass (36 to 110 ml. per kg. body weight), a high erythrocyte count (in one case up to 13,300,000 per c.mm.), a raised haemoglobin value (over 17 g. per 100 ml. in most cases, but only exceptionally with hyperchromia), leucocytosis (more than 20,000 per c.mm. in 20 cases), usually but not always a high platelet count, and hyperplasia of the erythroid, myeloid, and megakaryocytic series in the bone marrow. In treatment ^{32}P was given either orally or intravenously in the form of sodium phosphate in concentrations of 1 mc. per ml. of liquid. When given orally 15 to 50% is excreted, chiefly in the faeces, and when given intravenously 5 to 25% is excreted, chiefly in the urine. The actual dosage remains empirical, the purpose being to maintain the blood count as near normal as possible. At the Radium Institute the practice is to give 5 mc. of ^{32}P intravenously; if after 4 months there is little or no response the dose is repeated. A delayed response after 3 months, as shown by depressed activity of the bone marrow (estimated by means of a radioactive iron tracer test), contraindicates a further dose at this stage since this may produce anaemia and thrombocytopenia.

The observed increased incidence of chronic leukaemia or myelosclerosis in patients with polycythaemia treated with ^{32}P is attributed largely to the increased longevity of these patients, though reports of other investigators indicate that acute leukaemia may be caused by therapy with ^{32}P. Of 61 patients treated with ^{32}P alone, a full remission was obtained in 49 (80%), a partial remission in 9 (15%), and no response in 3 (5%). The average duration of remission was 2 years, the dose required varying between 5 and 20 mc., and the time taken to achieve remission 3 to 12 months. The results of deep x-ray therapy followed by ^{32}P compare favourably with those obtained with ^{32}P alone, but it is suggested that deep x-rays should be regarded as an adjunct in difficult cases rather than as a substitute for radioactive phosphorus.

Ethel Browning

1204. **Idiopathic Thrombocytopenic Purpura: an Evaluation of the Patterns of Response to Various Therapies**
W. B. SCHARFMAN, H. F. HOSLEY, T. HAWKINS, and S. PROPP. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 1875–1884, April 23, 1960. 1 fig., 18 refs.

The authors describe the results obtained in the treatment of idiopathic thrombocytopenic purpura in 50 consecutive cases admitted to Albany Hospital, New York, over a period of about 5 years. Of the 50 patients, 24 were children, and 21 of the 26 adults were females. Patients with secondary thrombocytopenia were excluded and the diagnosis was not considered proven unless megakaryocytes were plentiful in blood smears. Steroids in various doses were often effective even if there was no improvement in the platelet count. Transfusions of platelets or fresh blood were given in the presence of severe haemorrhage or to tide the patient over an operation. Splenectomy was never undertaken as an emergency measure; the authors found that there was no certain way of predicting which patients would be cured by surgery. Of the 47 patients for whom follow-up

data were available, 42 were in complete remission when last seen, which in 30 cases was over a year after discharge. There was one death and in 2 cases treatment was considered to be a failure. No definite scheme of treatment is recommended; in the authors' view the 7 case histories reported "illustrate the need for individualizing treatment". *P. C. Reynell*

1205. **Haemophilia: a Study of Its Laboratory, Clinical, Genetic and Social Aspects Based on Known Haemophiliacs in Finland.** [Monograph, in English]
E. IKKALA. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **12**, Suppl. 46, 1–144, 1960. 13 figs., bibliography.

ANAEMIA

1206. **Sickle-cell Anaemia Complicated by Megaloblastic Anaemia of Infancy**
J. E. MACIVER and L. N. WENT. *British Medical Journal* [*Brit. med. J.*] **1**, 775–779, March 12, 1960. 6 figs., 17 refs.

In a series of 50 cases of megaloblastic anaemia of infancy (some of great severity) due to folic acid deficiency in Jamaican children, 5 had sickle-cell anaemia—a highly significant incidence. As in other haemolytic syndromes associated with megaloblastosis, it is presumed that the excessive erythropoietic activity causes increased demands for haematopoietic substances which are likely to be deficient in the diets of Jamaican infants, while infection may also play a part. The infants responded maximally to folic acid. *R. B. Thompson*

1207. **Studies on Congenital Hemolytic Syndromes. III. Rates of Destruction and Production of Erythrocytes in Sickle Cell Anemia**
M. E. ERLANDSON, I. SCHULMAN, and C. H. SMITH. *Pediatrics* [*Pediatrics*] **25**, 629–644, April, 1960. 6 figs., bibliography.

The rates of destruction and of production of erythrocytes and of the production of haemoglobin were studied at New York Hospital–Cornell Medical Center in a group of 8 patients suffering from homozygous sickle-cell anaemia.

All patients were in a state of haematopoietic equilibrium, and the results were based on measurement of the life span of the patients' own erythrocytes labelled with radioactive chromium (^{51}Cr). The rates of destruction of the erythrocytes ranged from 5·6 to 20 times the normal and those of their production from 3·4 to 12·5 times the normal, while the rate of production of haemoglobin was 3·6 to 11·9 times the normal. These rates are greater than those found in patients with homozygous thalassaemia and congenital spherocytosis. The "compensation index" (that is, the rate of production of erythrocytes divided by their rate of destruction) ranged from 0·53 to 0·70. Comparison of the three congenital haemolytic diseases as seen in patients with similar compensation indices showed that the haematocrit value and haemoglobin concentration were lower in sickle-cell anaemia than in congenital spherocytosis, owing largely to failure of expansion of plasma volume in the latter disorder. In regard to homozygous thalassaemia, patients with similar compensation indices showed similar haemoglobin values but higher haematocrit values than patients with sickle-cell anaemia, a finding which is a reflection of the hypochromia of the erythrocytes in thalassaemia.

Studies of the localization of ^{51}Cr in various organs indicated sequestration of labelled erythrocytes in the liver in all patients with sickle-cell anaemia to a greater degree than in those with the other congenital haemolytic disorders. In 2 patients with splenomegaly radioactivity was increased in the splenic area; no splenic accumulation of radioactivity was found, however, after injection of normal erythrocytes labelled with ^{51}Cr, this excluding an extracorpuscular splenic haemolytic effect. In one patient who was studied during and after a painful crisis hyperhaemolysis did not occur, but there was slight contraction of the plasma volume during the crisis. Similar investigations were carried out on 2 patients with sickle-cell–thalassaemia disease and in 2 with sickle-cell–haemoglobin-C disease. In neither condition was the haemolytic defect as severe as in the usual case of sickle-cell anaemia.

[The original paper should be consulted for details of the techniques employed.] *J. L. Markson*

1208. **The Use of Radioactive Chromium in the Differential Diagnosis of Haemolytic Anaemia.** (Použití Cr 51 v diferenciální diagnostice hemolytických anémií)
V. KLEMENTOVÁ and J. DOHNÁLEK. *Československá pediatrie* [*Čsl. Pediat.*] **15**, 296–302, April, 1960. 6 figs., 8 refs.

Haemolytic anaemia is of two kinds, extracorpuscular and intracorpuscular. In a review of the literature available to them the authors found no mention of the differential diagnosis of these two types of the disease in children. At the Children's Hospital, Brno, Czechoslovakia, blood labelled with radioactive chromium (^{51}Cr) was given to 6 patients with haemolytic anaemia and 6 "haemolytically healthy controls" for purposes of differential diagnosis, the subsequent activities being followed in the two groups for a period of 3 weeks. In 3 patients this procedure was an aid in differential diagnosis, in 2 it was of some assistance, and in one patient it helped to exclude the diagnosis. The authors recommend that in treating such patients with blood transfusions the results must be evaluated by the use of crossed controls and by taking into account the results of other laboratory tests. *M. Hrusak*

1209. **Weight Loss in Pernicious Anaemia**
D. A. SEATON and A. GOLDBERG. *Lancet* [*Lancet*] **1**, 1002–1004, May 7, 1960. 2 figs., 11 refs.

The commonest features in pernicious anaemia are lack of energy, pallor, and dyspnoea, but in gastric carcinoma they are abdominal dyspepsia, anorexia, and loss of weight. Nevertheless, there is considerable overlap between the two conditions and patients with uncomplicated pernicious anaemia may be suspected of

suffering from cancer of the stomach. Of 50 consecutive patients admitted to the Western Infirmary, Glasgow, with proven pernicious anaemia, 36 had lost 14 lb. (6·3 kg.) or more in weight in the year before the condition was diagnosed. Occult blood in the faeces was not an uncommon finding. After treatment of the pernicious anaemia the lost weight was restored. In general, previously obese patients put on fat and lean patients predominantly lean tissue. It is suggested that a general metabolic effect of vitamin B_{12} (cyanocobalamin) is responsible for these changes and not, as has usually been supposed, the anorexia seen in some cases of untreated pernicious anaemia. In pernicious anaemia in relapse there is a poor correlation between blood volume and lean body mass, but this becomes normal after treatment. *R. B. Thompson*

1210. **Effect of Prednisone on B_{12} Absorption in Pernicious Anaemia.** [In English]
H. P. ØSTERGAARD KRISTENSEN and T. FRIIS. *Acta medica Scandinavica* [*Acta med. scand.*] **166**, 249–254, 1960. 4 figs., 7 refs.

Doig *et al.* (*Lancet*, 1957, **2**, 966; *Abstr. Wld Med.*, 1958, **23**, 440) found that some cases of megaloblastic anaemia responded to treatment with prednisolone. The mechanism of the effect of steroids upon pernicious anaemia, especially the effect of prednisone upon absorption of vitamin B_{12} (cyanocobalamin), was studied in 15 patients at the Frederiksberg Hospital, Copenhagen. Of the 15 patients (12 female aged 55 to 82 years and 3 male aged 71 to 77 years), 3 had not previously been treated, but the others were receiving adequate treatment. All were given 5 to 10 mg. of prednisone 4 times daily for periods ranging from 12 to 21 days. Vitamin-B_{12} absorption was estimated before, during, and after prednisone therapy from the amount excreted in the urine of a previously administered dose of radioactive vitamin B_{12}.

In 7 out of the 15 patients prednisone resulted in a marked increase in absorption of vitamin B_{12}. It appeared to influence absorption only in those cases in which a certain ability to absorb the vitamin had been preserved, indicating that prednisone acts by stimulating the production of the gastric intrinsic factor.
A. W. H. Foxell

1211. **The Mucosa of the Stomach and Small Intestine in Iron Deficiency**
A. RAWSON and F. D. ROSENTHAL. *Lancet* [*Lancet*] **1**, 730–731, April 2, 1960. 22 refs.

Degenerative changes in epithelial tissues are known to occur in iron-deficiency anaemia. Koilonychia, angular stomatitis, and glossitis are relieved by iron therapy, but gastric lesions, which are also common, often do not improve after treatment and there is some controversy as to whether the gastric lesions precede and favour the development of the anaemia or whether they are a result of the iron deficiency. To elucidate this question the authors, working at the Queen Elizabeth Hospital, Birmingham, have examined the mucosa of the upper small intestine of 10 patients with typical iron-deficiency anaemia to determine if any specific changes were present, arguing that if only normal mucosa were found the case for the primary responsibility of gastric changes for the anaemia would be strengthened. The 10 patients were selected on the basis of a fasting serum iron level of less than 40 μg. per 100 ml., no evidence of gastrointestinal bleeding or ulceration, " freedom from disease known to be associated with disturbances of iron metabolism ", and subsequent correction of the anaemia by oral iron alone. The intestinal mucosa specimens were obtained with a Shiner intestinal biopsy tube, while specimens of gastric mucosa were also taken with a Wood's biopsy tube. An augmented histamine test-meal was carried out.

It was shown that the small intestinal mucosa was normal in all 10 patients, but some gastric change in the form of gastritis, atrophy, or both occurred in all of them, being assessed as mild in one, moderate in 4, and severe in 5 cases. Achlorhydria was present in 3. The absorptive capacity of the small intestine was also estimated by means of an iron tolerance test and the results, though variable, were taken to show that absorption was unimpaired. The authors conclude that these findings strengthen the view that gastric abnormalities are at least one factor in the aetiology of iron-deficiency anaemia and not the result of it, and they suggest that these gastric mucosal abnormalities may be specially important when the amount of iron in the food is only " marginally adequate ". *M. C. G. Israëls*

1212. **Primary Iron-deficiency Anaemia in Young Men**
W. BRUMFITT. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **29**, 1–18, Jan. [received May], 1960. 2 figs., bibliography.

At the Cambridge Military Hospital, Aldershot, a haemoglobinometric survey was carried out photoelectrically on 2,000 young recruits to the Royal Army Medical Corps, a haemoglobin level of 80% (11·8 g. per 100 ml.) being chosen as the lower limit of normal. A value below this level was found in 22 (1·1%) of these recruits. This incidence and the distribution of values were strikingly similar to those found in a similar group investigated by the Medical Research Council in 1945. A comparative study by the author showed that in contrast the incidence of anaemia in 1,000 men of the Airborne Regiment who had completed their training and were very healthy was only 0·1%.

The 22 anaemic recruits and 8 other anaemic soldiers were further investigated in hospital. Chronic loss of blood was excluded by clinical, radiological, and biochemical tests, and the fact that no patient relapsed after treatment with oral iron was confirmatory evidence that there was no blood loss. Disorders of the alimentary tract such as idiopathic steatorrhoea were also excluded by fat balance tests and glucose tolerance tests. In addition there was no evidence of chronic infection in any of the patients. The main symptoms complained of were dyspnoea and lack of energy. These symptoms were much more frequent in men with haemoglobin values below 60% (8·9 g. per 100 ml.). None of the patients complained of dysphagia, anorexia, flatulence,

or diarrhoea, but one reported periodic sore tongue during the previous 3 years. The majority of patients had taken a good diet, but 4 of them disliked green vegetables and 2 disliked meat. The most common physical sign was conjunctival pallor, followed by facial pallor, and a systolic murmur. Many of the patients fell into the Registrar-General's Social Class III and in only one instance was there evidence of real financial hardship. The majority of the patients came from the North and the Midlands, some from the London area, but none came from the South.

The laboratory findings were all typical of iron-deficiency anaemia and it was noted that achlorhydria was more frequent in the more anaemic patients. Retesting of 17 of the patients after treatment showed that gastric secretion of acid had improved in 11, suggesting that the achlorhydria is secondary to the anaemia and reversible in milder cases. The results of other similar surveys are tabulated and the aetiology of iron-deficiency anaemia in males is discussed. Attention is drawn to the fact that in young men this anaemia develops between the ages of 18 and 20 years, after the period of adolescent growth. In patients who have a low intake of iron or suffer from poor absorption of the element this period of rapid growth may be the precipitating factor in the development of the anaemia.

R. F. Jennison

NEOPLASTIC DISEASES

1213. **Cerebral Hemorrhage in Leukemia**
S. N. Groch, G. P. Sayre, and F. J. Heck. *A.M.A. Archives of Neurology* [*A.M.A. Arch. Neurol.*] **2**, 439–451, April, 1960. 4 figs., 23 refs.

The incidence of cerebral haemorrhage in leukaemia was studied in 93 out of 235 cases of this disease in which necropsy was performed at the Mayo Clinic between 1945 and 1954. A complete examination, including study of the contents of the cranial cavity, was carried out in these 93 cases, and macroscopic cerebral haemorrhage was found in 46. Of the 93 patients, 65 (70%) had acute leukaemia, while of the 46 patients with cerebral haemorrhage, 42 (91%) had the acute form. Cerebral haemorrhages occurred equally frequently at all ages, were more commonly found in the cerebral hemispheres, especially in the white matter, and were often multiple. Haemorrhage outside the brain was more frequently found in patients with cerebral haemorrhage than in those without.

The platelet count was estimated in 41 patients with cerebral haemorrage and in 38 without; it was less than 60,000 per c.mm. in 31 of the patients in the former group and in 24 of those in the latter. The bleeding time and the prothrombin time were abnormal in all 12 cases in which these values were determined.

Histological examination of the brains showed infiltration of arterial walls and perivascular spaces with leukaemic cells. Some areas of vascular diapedesis of erythrocytes and fibrin exudation were often seen. Areas of vascular necrosis were rare. It is suggested that weakening of the blood-vessel walls, a lowered platelet count, and a decrease in plasma clotting factors contribute to cerebral haemorrhage in leukaemia.

David Phear

1214. **Leukaemia Imitating Poliomyelitis.** (Leukémie probíhající pod obrazem poliomyelitidy)
M. Macků and E. Bechinie. *Československá pediatrie* [*Čsl. Pediat.*] **15**, 344–352, April, 1960. 6 figs., 32 refs.

Poliomyelitis is a disease with a very varied symptom complex so that the diagnosis is often difficult. The authors describe a case of acute leukaemia in a boy aged 10 years. The first symptom was paresis of the 7th right cranial nerve. After admission to hospital meningism and abnormalities in the cerebrospinal fluid were revealed. Because the patient was in the incubation period and came from a district where poliomyelitis was present this disease was at first suspected. The blood count was normal at that time and it was not till a month later, when paralysis of the 7th cranial nerve developed also on the left side and an abnormal blood count was established, that the true diagnosis of acute lymphoblastic leukaemia was made. The patient died and the diagnosis was confirmed at necropsy. The nervous symptoms were due to luekaemic infiltration of the central nervous system. The authors emphasize the fact that in leukaemia neurological symptoms often precede the haematological ones and that the first sign of leukaemia may be a paresis of the 7th nerve or some other nervous disorder which may mask the underlying blood disease.

M. Hrusak

1215. **Chlorambucil in Erythrodermia**
J. Libánský and J. Trapl. *Lancet* [*Lancet*] **1**, 732–733, April 2, 1960. 11 refs.

Writing from Charles University, Prague, the authors recall that erythrodermia is a skin inflammation presenting a varied picture of irregular infiltration, sometimes pigmented, either dry or weeping, and accompanied by itching and burning. The syndrome is sometimes associated with changes in the lymphatic and blood-forming tissues resembling those seen in the reticuloses, such as enlargement of lymph nodes, splenomegaly, and the appearance of unusual monocytoid cells in the blood and bone marrow. Symptomatic treatment, including that with steroids, is disappointing. The relation to the reticuloses suggested the possibility that a cytostatic drug might be of value in its treatment and the authors here report the results obtained with "leukeran" (chlorambucil), a nitrogen-mustard type of drug that can be administered orally. They gave it in short courses in a dosage of 4·6 to 5·6 mg. per kg. body weight over 4 weeks. So far only 4 patients have been treated, but in all with excellent results. The itching was relieved and the affected skin returned to normal or almost normal colour. In one patient the remission has lasted for 2 years and in another 3 and 7 months respectively after two courses of treatment. A good result in a fifth patient is reported in an addendum. The authors agree that this is only a preliminary report, but since the results were so good they consider that their publication may be helpful to other workers.

M. C. G. Israëls

Respiratory System

1216. Unilateral Emphysema

R. F. Fouché, J. R. Spears, and C. Ogilvie. *British Medical Journal* [*Brit. med. J.*] **1**, 1312–1315, April 30, 1960. 4 figs., 7 refs.

The radiological and physiological findings in 7 patients with increased radiotranslucency of one lung are described in this paper from the London Hospital. All the patients gave a long history of recurrent cough and exertional dyspnoea, while 6 gave a history of pneumonia or pleurisy in earlier life. The increased translucency was in the right lung in 6 patients and in the left in one. There was diminished excursion of the diaphragm on the affected side, and deviation of the mediastinum towards this side on inspiration and away from it on expiration. Tomography showed decreased calibre of the main pulmonary artery and peripheral vessels on the affected side, usually most marked in the middle and lower zones, with an increase in calibre on the opposite side.

The physiological pattern differed only in degree from that seen in generalized emphysema. The relatively greater impairment of mixing efficiency was attributed to gross disparity in the ventilation rate between the two lungs. Normal values for diffusing capacity in 5 patients suggested successful adaptation to the increased blood flow by the unaffected remainder of the pulmonary capillary bed. In one case bronchospirometry showed hyperventilation of the abnormal lung accompanied by progressive over-inflation, with initially an increase in tidal volume and later a marked increase in rate and a decrease in tidal volume. For three minutes after this manœuvre there was no oxygen uptake from the abnormal lung, even though normal ventilation had been resumed.

It is suggested that the changes observed may be the result of transient bronchial obstruction during earlier respiratory infections. *B. Golberg*

1217. Indirect Estimation of Arterial CO_2 Tension in Emphysema

L. Feinmann, D. J. Newell, and G. B. Pendlenton. *Thorax* [*Thorax*] **15**, 43–46, March [received May], 1960. 4 figs., 15 refs.

The method of indirect estimation of carbon dioxide tension of arterial blood herein described is based on the breath-holding technique of equilibrating alveolar CO_2 with the CO_2 of mixed venous blood. In a healthy subject the plateau of " alveolar " CO_2 measured in a single expiration at rest is in equilibrium with arterial CO_2, and its tension can be used as an indirect estimate of the latter; but the absence of a plateau in emphysema makes this impossible.

During a tidal expiration two measurements are simultaneously recorded on an oscilloscope: (1) vertically, continuous CO_2 content by an infra-red analyser, and (2) horizontally, volume expired. The curve so obtained is photographed against a calibrated scale. The manœuvre is repeated after breath-holding for 2½, 5, and 10 seconds. Breath-holding produces a plateau on the CO_2 concentration curve, and the corresponding pCO_2 correlates well with the pCO_2 of arterial blood (derived from *p*H and CO_2 content of arterial blood samples). The first curve, obtained without breath-holding, demonstrates whether a raised arterial pCO_2 is due to uneven ventilation or to hypoventilation alone.

The apparatus is relatively expensive and takes some time to set up and calibrate, but once this has been done a large number of patients can be examined quickly and without discomfort. The technique is easier to carry out than arterial blood gas analysis and its accuracy is sufficient for clinical purposes. *Bernard J. Freedman*

1218. The Respiratory Response to Carbon Dioxide in Health and in Emphysema

D. Brodovsky, J. A. Macdonell, and R. M. Cherniack. *Journal of Clinical Investigation* [*J. clin. Invest.*] **39**, 724–729, May, 1960. 4 figs., 11 refs.

At the General and Deer Lodge Hospitals (University of Manitoba), Winnipeg, the respiratory response to carbon dioxide was studied in 2 female and 10 male normal subjects aged 19 to 34 and 10 emphysematous patients, all males, aged between 43 and 73 years. Arterial carbon dioxide tension (pCO_2) was varied by altering the amount of dead space in a closed-circuit spirometer through which the subject breathed. The pCO_2 was measured directly in the emphysematous patients and estimated from the end-tidal pCO_2 in the normal subjects. An increase in pCO_2 caused a rise in minute volume in both groups of subjects, but to a lesser extent in the emphysematous. The resulting increase in oxygen consumption was the same in each group.

The increase in the mechanical work of breathing was calculated by plotting oxygen consumption against minute ventilation; such increase with a rising pCO_2 was much less marked in the emphysematous patients than in the healthy controls. The authors suggest that incremental changes in total mechanical work provide a more accurate measure of respiratory response to CO_2 than do changes in minute volume or oxygen consumption, and the present results show that the response is lower in emphysematous than in normal subjects. Among those emphysematous patients with CO_2 retention at rest the response was even lower. *D. Goldman*

1219. Subcutaneous Gas Equilibration in Clinical Practice

P. Forgacs. *Thorax* [*Thorax*] **15**, 37–42, March [received May], 1960. 5 figs., 9 refs.

The clinical application of subcutaneous gas equilibration is discussed in this paper from the Brook General Hospital, Shooters Hill, London. Air filtered through

cotton wool is drawn into a 10-ml. syringe with 2-way tap and injected into the subcutaneous tissues of the forearm. A depot of 50 ml. yields several samples during the next 12 hours, but up to 100 ml. can be more easily located the following day. Equilibration with tissue carbon dioxide takes 80 minutes, during which time the forearm is kept warm. A small sample is taken when required thereafter by subcutaneous puncture, suction being avoided, and analysed for CO_2 content in a Scholander gas analyser. The percentage is converted directly to pCO_2.

There is, on the whole, a good correlation between subcutaneous pCO_2 and the pCO_2 of arterial blood measured by bubble equilibration, the level of former tending to be lower by a few mm. Hg. Subcutaneous gas is less liable to short-term fluctuations due to transitory ventilatory changes than is arterial blood, owing to the time taken for equilibration between arterial-blood and subcutaneous pCO_2. It more truly reflects the dissolved CO_2 stores of the body. The method is therefore especially valuable in the management and ventilatory control of patients receiving mechanical artificial respiration and in assessing progress in cases of acute and chronic respiratory failure due to bronchitis and emphysema.

[This simple technique should prove of value to those who are concerned to find quick and easy methods suited to routine hospital practice of estimating hypercapnia in hypoventilated patients.] *Bernard J. Freedman*

1220. **Physiological Factors Affecting Airway Resistance in Normal Subjects and in Patients with Obstructive Respiratory Disease**
J. Butler, C. G. Caro, R. Alcala, and A. B. Dubois. *Journal of Clinical Investigation* [*J. clin. Invest.*] **39**, 584–591, April, 1960. 6 figs., 13 refs.

In normal subjects airway conductance (which is the reciprocal of airway resistance and is here defined as the rate of air flow at the mouth for unit pressure difference between the alveoli and the mouth) increases at larger lung volumes; yet in patients with asthma or emphysema, who are breathing with a large functional residual capacity (F.R.C.), it is reduced. The authors, working at the Graduate School of Medicine, University of Pennsylvania, Philadelphia, therefore tested the effects of various factors which might influence airway conductance both in healthy subjects of various ages and in patients with bronchitis and emphysema, the factors tested being restriction of the chest produced by strapping, bronchomotor drugs, exercise, the breathing of different concentrations of oxygen and carbon dioxide, forced breathing, and old age.

Airway resistance and thoracic gas volume were first measured during panting in the sitting position by using an upright whole-body plethysmograph. In 6 healthy young subjects repeat measurements of airway resistance when panting at about the F.R.C. were made at 20-minute intervals during a 2-hour period. They showed little variation with time. The airway resistance of 10 healthy elderly subjects ranging in age from 75 to 90 years was similar to that of the younger people, although the old subjects showed a reduction in maximum breathing capacity and maximum flow rates compared with the young. The authors suggest that reduction in the maximum pressure generated by the respiratory muscles and the increased resistance of the lung tissue in the elderly probably contributed to the diminution of the maximum flow rates in this group.

Airway conductance was found to depend upon the elastic pressure of the lung rather than on lung volume. In 10 normal subjects there was a change in the pressure–volume curve of the lungs after the chest and abdomen were tightly strapped, and at each lung volume the airway conductance was greater after chest strapping than before it. But after removal of the strapping the lung elastic-pressure–lung-volume curve formed a large hysteresis loop which was similar to that of the airway-conductance–lung-volume curve on its return to normal. After exercise airway conductance was slightly increased since the subjects were breathing in a "slightly more inspiratory position". Forced breathing of pure oxygen did not affect airway resistance whether measured immediately or at intervals during breathing of the gas for 5 to 6 hours, nor did breathing 4 to 10% carbon dioxide in air over periods of up to 10 minutes. In 8 asthmatic or emphysematous patients the airway conductance at the F.R.C. was reduced. Change in conductance per unit change in volume was less than normal and the failure of the increase in F.R.C. of these patients to restore normal conductance appeared to be due to the lower slope of their conductance–volume relationship. Bronchodilator drugs altered the curve of the airway conductance versus lung volume not only in asthmatic patients and to some extent in emphysematous patients, but also in the normal subjects. Exercise and forced breathing increased airway resistance in several patients with mild asthma.

When airway conductance was reduced by disease there was less than the normal change in conductance from alteration of lung elastic pressure; the distensibility of the airways appeared to be decreased. Further, both the lung elastic pressure and the volume at which airway conductance approached zero (obtained by extrapolation) were increased in the patients, suggesting that there was some gas-trapping at greater than normal transpulmonary pressures and lung volumes. Bronchodilator drugs appeared both to improve airway distensibility and to reduce the volume at which conductance approached zero. *P. Hugh-Jones*

1221. **Eosinophils and Neutrophils in Sputum and the ESR with Particular Reference to Asthma.** [In English] H. Colldahl. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **15**, 124–129, 1960. 3 figs., 9 refs.

A study has been performed of the presence of neutrophil and eosinophil cells in the sputum—principally in cases of asthma, but also of other diseases of the lungs and bronchial tract. In conjunction with the erythrocyte sedimentation rate the cell distribution in the sputum can provide information of value in diagnosis and therapy. It might well be used as a routine measure in the investigation of lung diseases.—[Author's summary.]

Otorhinolaryngology

1222. **Pure-tone Thresholds of Professional Pianists**
G. E. ARNOLD and F. MISKOLCZY-FODOR. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **71**, 938–947, June, 1960. 8 figs., 19 refs.

At the New York Eye and Ear Infirmary the authors have undertaken an examination of the possible hearing loss in musicians. In this paper they report on the hearing acuity of 30 professional pianists, 10 men aged 60 to 69 years and 20 women aged 60 to 80 years. There was no evidence of traumatic hearing loss; on the contrary the acuity was better than that found in the general population of the same age group. As the average loudness level of the piano is only about 70 decibels, and the peak of loudness during occasional *fortissimo* passages does not exceed 95 decibels acoustic damage is unlikely. The players of brass instruments and tympanists, however, are exposed to higher levels, and it is urged that the hearing acuity of such musicians should be investigated. *F. W. Watkyn-Thomas*

1223. **Diagnosis and Treatment of Vascular Insufficiency Causing Perceptive Deafness**
T. J. WILMOT and J. C. SEYMOUR. *Lancet* [*Lancet*] **1**, 1098–1102, May 21, 1960. 4 figs., 4 refs.

At the Tyrone and Fermanagh Group of Hospitals, Northern Ireland, 317 cases of perceptive deafness seen during the period 1953–8 which were not of congenital origin or due to viral infection, physical acoustic trauma, labyrinthitis, or old age were investigated. Some were of sudden and some of gradual onset, some were associated with vertigo and some with fluctuation in hearing level. There were 174 males and 142 females.

Of these 317 cases, the hearing was definitely improved within 24 hours in 85, but was not improved in 232, by blocking the sympathetic chain at or above the level of the stellate ganglion. It is considered that this procedure increases the blood supply to the ear. It was found that patients whose deafness was of recent onset or in whom the hearing fluctuated or who suffered from vertigo showed a greater tendency to benefit from sympathetic block. But such a block does not improve the hearing in senile deafness, acoustic trauma, occupational deafness, or deafness associated with hypertension.

The treatment of early cases with slight low-tone unilateral deafness and tinnitus is mainly by firm reassurance and simple sedation. That of the acute case with severe vertigo, tinnitus, and fluctuation in hearing is by immediate stellate block followed by large doses of a vasodilator drug such as nylidrin hydrochloride (up to 30 or 40 mg. daily). Cases of longer standing should first be treated with a vasodilator drug for one month; if not fully relieved by this treatment but showing some improvement they should then be subjected to cervical sympathectomy. When these measures fail resort must be made to sedation and the administration of antihistaminic or tranquillizer drugs, but these should not be used before an exact diagnosis has been made since they tend to invalidate the response to audiometric and caloric tests. The authors are not satisfied that a low-fluid or a low-salt diet is of any benefit. *Norman W. MacKeith*

1224. **Experiences with the Fenestra Ovalis Technique of Shea. A Preliminary Clinical and Experimental Report**
D. MYERS, S. D. ERULKAR, W. D. SCHLOSSER, L. PRATT, and R. A. WINCHESTER. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St Louis)*] **68**, 996–1016, Dec., 1959. 9 figs., 3 refs.

The results of Shea's operation for otosclerosis in more than 100 cases are analysed from Temple University Medical Center, Philadelphia. This operation consists in the removal of a large part of the footplate of the stapes and the crura and replacement by a polythene strut lying on a piece of vein wall which is made to cover the oval window and the gap in the footplate.

The results are most encouraging, for of the 95 patients on whom routine postoperative hearing tests were performed, 69 reached the 30-db level for speech frequencies, 37 showed complete closure of the air–bone gap, and 33 fell within normal limits of hearing. It is to be remembered that this operation is usually undertaken only in severe and widespread otosclerosis. The longest period of observation was 12 months. *William McKenzie*

1225. **An Audiometric Study of Two Hundred Cases of Subjective Tinnitus**
G. F. REED. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **71**, 84–94, Jan., 1960. 2 figs., 40 refs.

From the Massachusetts Eye and Ear Infirmary, Boston, the author reports the results of an audiometric study of 200 patients who were all suffering from subjective tinnitus severe enough to make them seek advice. The series included only 15 cases of otosclerosis, since most such cases were referred to a separate clinic. Special apparatus was devised to measure the frequency and the apparent intensity of the tinnitus by checking the sensation against measured sounds. Nearly one-quarter of the patients could match their tinnitus against a pure tone, contrary to the finding of Fowler (*Arch. Otolaryng. (Chicago)*, 1944, **39**, 498). Over half the patients (56%) matched the tinnitus against the 2,000- to 6,000-cycle range. The "loudness" was seldom as high as the patients suggested. There was no apparent sex difference, but the incidence of tinnitus definitely increased with age. Although 90% of the patients had some loss of hearing, only about one-half were conscious of it. [The diagnosis of the cases is not altogether convincing, particularly the assumption of a cochlear origin rather than a central origin in 75% of the cases, but it is clear that Eustachian or middle-ear trouble was a very infrequent cause, there being only 11 such cases among the 200.] *F. W. Watkyn-Thomas*

Urogenital System

1226. **The Determination of Renal Function by Sergosin Excretion following Its Intravenous Administration for Urography.** (Определение функции почек по выделению сергозина, введенного внутривенно с целью урографии)
A. V. Mahrov. *Урология* [*Urologija*] **25**, 30–34, March–April, 1960. 1 fig.

"Sergosin" is an iodine-containing radio-opaque substance, and its concentration in urine can be determined very accurately. It can therefore be used for both urographic and chemical methods of determining renal function. For the early determination of renal function in patients with osteoarticular tuberculosis the author used a combined method of diagnosis—catheterization of ureters, urography, and determination of sergosin excretion from each kidney. Such a combination of methods helps to establish an earlier and more accurate diagnosis of renal tuberculosis. In this way the early stage of renal tuberculosis was diagnosed in 45 patients.

The determination of renal function by sergosin excretion from the kidneys following its intravenous administration for urography proved to be more accurate than the indigo-carmine and Zimnitskii's methods. The author gives a graph of the excretion of sergosin in a normal patient compared with that of a patient with bilateral renal tuberculosis. *N. Hopewell*

1227. **Localization of Gamma-globulin in the Diseased Kidney**
P. Freedman, J. H. Peters, and R. M. Kark. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **105**, 524–535, April, 1960. 6 figs., 23 refs.

The authors report from the University of Illinois, Chicago, a study of the localization of γ globulin in sections of renal tissue from 43 patients, obtained in 34 cases by percutaneous biopsy and in 9 post mortem. The γ globulin was detected with fluorescent rabbit anti-human γ-globulin conjugate. The specificity of staining was confirmed by the diminution of fluorescence by unconjugated antibody and the failure of anti-rabbit γ globulin to stain the sections. Biopsy and fresh post-mortem material gave similar results.

Sections from the 9 patients without renal disease showed virtually no specific staining. In 7 patients with acute glomerulonephritis diffuse staining of the glomerular capillary walls occurred; in 3 cases there was staining of small blood vessels and in one some staining of the tubular epithelial cells; in one convalescent case the staining was slight, but sections from one with evidence of progressive disease stained heavily. Weak focal staining of the glomerular capillary wall occurred in 2 patients with proliferative glomerulonephritis. Staining was also seen in sections from all 5 patients with membranous glomerulonephritis, but not in those from one patient with combined proliferative and membranous nephritis. In one case of chronic glomerulonephritis the glomeruli, tubules, and blood vessels stained, and in 3 patients with diabetic nephropathy there was also marked staining of these elements and of the characteristic nodular deposits in the glomeruli. All 4 cases of scleroderma showed staining of the small blood vessels, but the renal glomeruli were involved in only 2. Staining was also noted in one patient with periarteritis nodosa, one with amyloid disease, and in 7 out of 8 patients with systemic lupus erythematosus.

Elution at acid *p*H diminished the fluorescence of kidney sections. It was found that γ globulin could be demonstrated in the 15-minute eluate of glomerulonephritic kidneys, but not of normal kidneys. However, the 150-minute eluate of both normal and diseased kidneys contained γ globulin. The authors suggest that the renal localization of γ globulin is due either to absorption by damaged renal tissue or to a specific antigen–antibody combination. It is their opinion that the elution studies slightly favour the second view. *G. L. Asherson*

1228. **A Study of the Association of Group A Streptococci with Acute Glomerulonephritis**
S. H. Bernstein and M. Stillerman. *Annals of Internal Medicine* [*Ann. intern. Med.*] **52**, 1026–1034, May, 1960. 1 fig., 29 refs.

At the Long Island Jewish Hospital, New Hyde Park, New York, the results of culture of throat swabs and estimation of the antistreptolysin titre taken in combination gave evidence of preceding streptococcal infection in each of 51 patients suffering from acute glomerulonephritis. A raised antibody level was present in 92% of the group, and relevant organisms were isolated in 61%. Of the 30 strains of Group-A haemolytic streptococci identified, 18 were of Type 12, 4 of Type 49, one each of Types 5, 18, 19, and 41, and 4 were untypable. Type 12 was the dominant streptococcus in the community from which the patients were drawn.

Further investigation revealed that many of the unaffected relatives of the patients also harboured similar streptococci; of one pair of identical twins both members had throat infections with Type-12 streptococcus, but only one had clinical nephritis. The isolation of streptococci from half the patients at the stage of nephritis is held to justify giving an adequate course of penicillin at this stage. Of the 51 patients, 31 were aged 10 or under and 11 were over 20. None of the patients showed evidence of renal damage after the acute attack had subsided. *D. A. K. Black*

1229. **The Pathophysiology of the Nephrotic Syndrome.** [Review Article]
D. A. Adams. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **106**, 117–142, July, 1960. 5 figs., bibliography.

Endocrinology

1230. **The Influence of Certain Hormone Preparations on the Absorption of Glucose by the Small Intestine.** (Влияние некоторых гормональных препаратов на всасывание глюкозы в тонком кишечнике)
E. E. Jaremko. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **6**, 15–17, May–June, 1960. 3 figs., 5 refs.

This paper describes experiments carried out on 3 dogs in which a loop of small intestine had been isolated and into which 15 ml. of isotonic solution (5·6%) of glucose was injected every 15 minutes. From the concentration of glucose in the fluid and the volume of fluid remaining in the loop the amount of glucose absorbed could be calculated. Each experiment lasted 4 hours; in the first 2 hours the normal absorption of glucose in each individual animal was measured, and then after administration of the hormone under test glucose absorption was estimated during the next 2 hours. In all, 58 experiments in three series were performed.

In the first series the effect of pituitrin and ACTH (corticotrophin) was investigated. The injection of 3 units of pituitrin resulted in a definite fall in glucose absorption, from 2,306 to 1,814 mg. in the 2 hours, whereas 10 units of ACTH caused only an insignificant fall in some experiments. The use of ACTH–zinc phosphate in a 12-hour experiment produced a slight fall in absorption from 2,389 to 1,779 mg. in 2 hours, this being followed by a steady rise over the next 4 hours to 2,455 mg., after which the rate of absorption fell to 1,340 mg. in the next 4 hours.

In the second experiment, in which cortisone and adrenaline were tested, the introduction of 1 ml. of cortisone [presumably 25 mg., but this is not stated] produced a slight fall in absorption (from 1,857 to 1,617 mg.), while 1 ml. of 1:1,000 adrenaline caused a much more pronounced fall (from 1,952 to 1,416 mg.). In the third series of experiments thyroxine and insulin were tested, the dosage being 0·5 ml. of Schering–Kalbaum thyroxine and 15 units of insulin. Both these hormones caused a considerable rise in absorption—from 1,609 to 1,943 mg. in the case of thyroxine and from 2,026 to 2,544 mg. in the case of insulin. *L. Firman-Edwards*

1231. **Assessment of the Functional Capacity of the Adrenal Cortex. II. Clinical Application of the ACTH Test**
G. Birke, E. Diczfalusy, and L. O. Plantin. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **20**, 593–608, April, 1960. 5 figs., 24 refs.

In a previous paper (*J. clin. Endocr.*, 1958, **18**, 736) the authors described an improved method of measuring the functional reserve capacity of the adrenal cortex, based upon the estimation of the urinary excretion of 17-hydroxycorticosteroids before and after administration of corticotrophin (ACTH). In the present paper from Karolinska Sjukhuset and King Gustaf V Research Institute, Stockholm, they report the application of this method to the study of 100 cases of established or suspected adrenocortical disease.

Of 8 patients with cortical hyperplasia (manifestations of either Cushing's or the adrenogenital syndrome) 6 gave an exaggerated response to injection of ACTH. In 4 patients with benign cortical adenomata and one with a cortical carcinoma there was no response or only a weak one. None of the 11 patients with Addison's disease, including 3 in whom the resting excretion of 17-hydroxycorticosteroids was in the low normal range, showed any response to ACTH stimulation. Similarly, in 3 patients who had undergone bilateral adrenalectomy there was no increase in hydroxycorticosteroid excretion following ACTH administration, but 5 patients with primary hypopituitarism and lowered resting hydroxycorticosteroid levels showed a normal or near-normal response.

ACTH stimulation was also tried in 66 patients in whom adrenocortical hypofunction was suspected on the basis of the presence of at least one of the cardinal symptoms of Addison's disease—loss of weight, weakness, hyperpigmentation, hypotension, hypoglycaemia, and disturbed electrolyte and/or water balance. Few of these patients gave a completely negative response. A diminished response was observed in 43, and most (90%) of these had two or more suggestive symptoms; only 40% of those with one symptom, usually weakness, showed a low excretion of corticosteroid in response to ACTH.

The authors suggest that if this technique is used and the results are recorded logarithmically, a valuable method of assessing the endocrine capacity of the adrenal cortex is available. The results of this investigation provide support for the existence of the disease entity of impaired adrenocortical reserve.

H.-J. B. Galbraith

1232. **Post-pubertal Adrenal Virilism with Biochemical Disturbance of the Congenital Type of Adrenal Hyperplasia**
R. V. Brooks, D. Mattingly, I. H. Mills, and F. T. G. Prunty. *British Medical Journal* [*Brit. med. J.*] **1**, 1294–1298, April 30, 1960. 5 figs., 20 refs.

From St. Thomas's Hospital Medical School, London, the authors report the cases of 3 young women aged 18 to 20 who were suffering from a manifestation of the adrenogenital syndrome apparently of the type found in congenital adrenal hyperplasia but appearing for the first time after the onset of puberty. All 3 patients developed hirsutism and 2 of them acne after the establishment of normal menstruation. All of them had poorly developed secondary sexual characteristics; biochemical investigation showed their urine to contain an excess of pregnanetriol and this excess was increased further by

the administration of corticotrophin. In addition, the urine in all 3 cases showed an excess of 11-oxo-pregnanetriol while metabolites of cortisol were relatively deficient.

In the authors' opinion this type of adrenogenital syndrome is basically a congenital biochemical lesion which is latent until the underlying defect is brought to light by the changing conditions of puberty. It is emphasized that for the present " this group of patients can only be defined in biochemical terms and distinguished from patients with hirsutism of different origin ", as previously described (Prunty *et al.*, *Brit. med. J.*, 1958, **2**, 1554; *Abstr. Wld Med.*, 1959, **26**, 35). *J. Warwick Buckler*

1233. **Treatment of Simple Hirsutism, Including the Hirsute Type of Stein–Leventhal Syndrome**
D. Mattingly, I. H. Mills, and F. T. G. Prunty. *British Medical Journal* [*Brit. med. J.*] **1**, 1298–1300, April 30, 1960. 1 fig., 13 refs.

In this further paper from St. Thomas's Hospital Medical School [see Abstract 1232], the authors report the results of treating 21 patients with simple hirsutism and 3 with hirsutism of the Stein–Leventhal type. Treatment consisted in the administration of prednisone in an average dosage of 10 mg. per day, combined usually with ethinyl oestradiol in doses varying from 0·05 mg. to 0·3 mg. daily for 3 weeks out of every 4; the prednisone was administered for periods varying from 4 to 39 months.

Six patients improved markedly on this regimen and there was doubtful improvement in a further 9. The 3 patients with the Stein–Leventhal syndrome were equally divided among the three categories (defined) of 17-ketosteroid suppression.

The authors conclude that while treatment of this type may occasionally benefit these patients, the frequency of beneficial results is not such as to justify routine administration of steroids in all cases of hirsutism. It is unfortunate that as yet it is not possible to predict which particular individual is likely to respond to this therapeutic regimen. *J. Warwick Buckler*

PITUITARY GLAND

1234. **Antidiuretic Properties of Hydrochlorothiazide in Diabetes Insipidus**
C. W. H. Havard and P. H. N. Wood. *British Medical Journal* [*Brit. med. J.*] **1**, 1306–1308, April 30, 1960. 2 figs., 20 refs.

From St. Bartholomew's Hospital, London, the authors report one case of diabetes insipidus in which hydrochlorothiazide was used as an antidiuretic. They confirmed the findings of previous workers that the administration of hydrochlorothiazide in a dose of 50 mg. twice daily and subsequently 100 mg. on alternate days results in a marked reduction of urinary volume. This reduction was preceded by a large urinary loss of sodium and chloride on the first day of therapy. As a result of this loss of sodium and water the plasma volume was reduced by 20% and the body weight decreased by 5 lb. (2·3 kg.). The glomerular filtration rate was reduced by 65%. It is possible that the drug had a direct and primary action on the glomerular filtration rate which was not dependent upon the electrolyte loss.

The authors conclude that although hydrochlorothiazide reduces the urinary volume and consequently relieves the patient of the more distressing symptoms, it is not superior to vasopressin and is not, in fact, the treatment of choice. Its use should be reserved for those patients who cannot tolerate vasopressin either in the form of snuff or by injection. *J. Warwick Buckler*

1235. **Clinical Results of Treatment of Diabetes Insipidus with Drugs of the Chlorothiazide Series**
J. D. Crawford, G. C. Kennedy, and L. E. Hill. *New England Journal of Medicine* [*New Engl. J. Med.*] **262**, 737–743, April 14, 1960. 5 figs., 17 refs.

Working in the Department of Experimental Medicine, University of Cambridge, the authors have studied the effects of chlorothiazide and related drugs on 7 patients with diabetes insipidus, of whom 6 had the vasopressin-deficient form of the disease and the 7th the congenital, nephrogenic form.

In all 7 patients, 2 hours after ingestion of the drug, there was an abrupt rise in the urinary sodium excretion and to a lesser degree of potassium excretion, accompanied by chloride as the major anion. These increases were accompanied some 4 to 6 hours after taking the drug by a steady decline in urinary flow with an abrupt rise in osmolarity of the urine. The body weight decreased by about 1,100 g. in 24 hours as a result of the loss of sodium. All the patients excreted sodium and most of them also water in excess of intake for 6 to 24 hours, after which an equilibrium was reached and the body weight returned to pre-treatment values. It was clear, however, that the degree of control possible with these drugs in the patient sensitive to vasopressin was inferior to that achieved by replacement therapy. A further study of the effect of combined therapy in 4 of the patients showed that 2 who were well controlled by means of vasopressin snuff taken 4 times daily were equally well controlled when given the snuff once daily together with chlorothiazide. The third patient, who had been partially refractory to vasopressin, did better under combined therapy, while the fourth, who had become refractory to continuous hormone replacement therapy, showed a higher urinary osmolarity on treatment with the snuff and chlorothiazide. In contrast to these effects of chlorothiazide it was found in these patients that other diuretics such as acetazolamide, mersalyl, and dichlorphenamide, caused an abrupt increase in the urinary flow.

The authors conclude that there is no necessity to change over to chlorothiazide in those patients responsive normally to vasopressin, particularly in view of the known potential toxic effects of chlorothiazide on the bone marrow and in causing potassium deficiency. On the other hand, in those patients refractory to vasopressin and those with the nephrogenic type of diabetes insipidus the wider use, after further investigation, of chlorothiazide appears desirable. The mode of action of chlorothiazide and analogues in these patients is not

clear, except that it is not due simply to the diuretic action of these drugs, nor to gross reduction of the body sodium content or of the glomerular filtration rate, nor to a failure of the necessary substrate sodium to reach the site of free water formation. Studies briefly reported by the two first-named authors (*Nature* (*Lond.*), 1959, **184**, 1492) suggest that the action of chlorothiazide depends on blockade at the kidney of adrenal mineralocorticoids. *A. Gordon Beckett*

THYROID GLAND

1236. **Human Foetal Thyroglobulin, with Particular Reference to the Aetiology of Hashimoto's Disease**
B. RUEBNER, G. VAN LEEUWEN, and L. KORNGOLD. *Lancet* [*Lancet*] **1**, 1108–1109, May 21, 1960. 1 fig., 11 refs.

At Dalhousie University, Halifax, Nova Scotia, this study was undertaken in an attempt to determine the age at which the foetal thyroid gland begins to contain thyroglobulin, fresh thyroid glands from 16 foetuses varying in age from about 12 to 40 weeks being examined. In addition to histological examination, thyroglobulin was tested for by an Ouchterlony technique. It was found that a substance antigenetically indistinguishable from thyroglobulin was present in the foetal thyroid from the age of 23 weeks. There was no good correlation between the age of the foetus and the proportion of colloid-containing acini. These findings are discussed with reference to the aetiology of Hashimoto's disease.
Norval Taylor

1237. **Changes in Serum Protein-bound Iodine, Serum Cholesterol and the Radioactive Iodine Excretion Test in Thyrotoxicosis Treated with Radioactive Iodine.** [In English]
R. HAKKILA, B. A. LAMBERG, and C. A. HERNBERG. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **33**, 593–602, April, 1960. 6 figs., 36 refs.

A study is reported from the University of Helsinki of the changes in the serum protein-bound iodine (P.B.I.) level, the serum cholesterol level, and the urinary excretion of radioactive iodine (^{131}I) in 144 patients with thyrotoxicosis, 98 of whom had nodular goitre and 34 a diffuse goitre, while in 12 the thyroid gland was not palpable.

In the majority of the patients the serum levels of P.B.I. and cholesterol showed a close correlation with the clinical state, but there was a discrepancy in a few cases. This was especially seen as a temporary feature in the intermediate stage of treatment, when euthyroidism was accompanied by low serum P.B.I. and high serum cholesterol levels. The authors state that these cases probably represent temporary hypothyroidism. In most cases the urinary excretion of ^{131}I gradually increased, although a few patients showed a high initial excretion due to radiation injury. In the intermediate stage of treatment excretion was markedly elevated in some cases, as a result, probably, of blocking of the thyroidal uptake mechanism. Sometimes excretion was low in the later stage without accompanying hyperthyroidism, indicating a limited thyroidal iodine pool with a rapid turnover. In the authors' view measurement of the excretion or the thyroid uptake of ^{131}I in the early phase after treatment will give some information concerning the radiation injury to the thyroid gland, but these values are unreliable as tests of thyroid function. They conclude that in patients with hyperthyroidism estimation of the serum P.B.I. and serum cholesterol levels at intervals after ^{131}I treatment will generally give an accurate picture of the course of the remission.
D. G. Adamson

1238. **Thyrotrophin as an Aid in Radioiodine Treatment.** [In English]
J. EINHORN and L. G. LARSSON. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **34**, 129–136, May, 1960. 24 refs.

The effect of thyrotrophic hormone (thyrotrophin) on the uptake of radioactive iodine (^{131}I) by the thyroid gland was studied at Karolinska Sjukhuset, Stockholm, in 15 patients who had clinical hyperthyroidism but whose thyroidal uptake of ^{131}I was low. After administration of thyrotrophin, which, in the majority of cases, was given as a single dose of 5 *U.S.P.* units some 18 hours before the ^{131}I, there was a definite increase in the uptake of the isotope by the thyroid gland. Of the 15 patients, 8 had previously received treatment with iodine. Large nodular goitres were present in 12 and diffuse enlargement of the gland in 2. Only in one patient, who was given 4 injections of thyrotrophin, was there any increase in hyperthyroidism. Repeated studies showed a decreasing effect of the thyrotrophin in terms of ^{131}I uptake, indicating that the effect of the hormone was transient. Similar results were obtained in 6 patients who had nodular goitre and who had remained hyperthyroid, but in whom the ^{131}I uptake by the gland was low 3 to 6 months after ^{131}I therapy. In 3 euthyroid patients administration of thyrotrophin was followed by an increase in the ^{131}I uptake by the gland which had previously been subnormal.

The authors conclude that when ^{131}I therapy is indicated in the presence of a low uptake of the isotope injection of thyrotrophin is of value by facilitating the concentration of ^{131}I by the thyroid gland.
Charles Rolland

1239. **The Endocrine Eye Lesion in Hyperthyroidism: Its Incidence and Course in 165 Patients Treated for Thyrotoxicosis with Iodine^{131}**
H. E. HAMILTON, R. O. SCHULTZ, and E. L. DE GOWIN. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **105**, 675–685, May, 1960. 8 figs., 18 refs.

The incidence and clinical course of eye abnormalities in 165 thyrotoxic patients treated with radioactive iodine (^{131}I) are described in this paper from the Thyroid Clinic of the College of Medicine, State University of Iowa. The patients (27 male and 138 female, aged 14 to 80 years) were observed for one to 5 years after the thyrotoxicosis had been controlled. Exophthalmos and the other components of the eye lesion—lid retraction, oedema with conjunctival injection and excessive lacrimation, recent ocular palsies, pain, photophobia, water-

ing, diplopia, and disturbed visual acuity—are separately analysed.

Of the 165 patients, 120 had some component of the eye lesion. The lesion was initially severe in 18 and moderately severe in 46. After treatment ocular protrusion increased or was unchanged in 91%, while other eye signs decreased or disappeared also in 91%. Significant eye signs or symptoms persisted in 15 patients at the end of treatment. Diplopia was present in 27 patients before treatment and in only 8 afterwards. Rapid control of thyrotoxicosis was more frequently associated with improvement in the eye lesions than was slow control, in which ^{131}I treatment had to be repeated. The eye signs or symptoms became worse in 9 patients during treatment and in 14 patients whose treatment was incomplete.

Pretibial myxoedema was associated with a high incidence of eye lesions. Of 22 patients in whom myxoedema developed after treatment, 3 showed a temporary deterioration of the eyes, which, however, improved again when thyroid extract was given. Eye lesions were more frequent in patients with diffuse goitre than in those with toxic nodular goitre. *David Phear*

1240. **Triiodothyronine in the Diagnosis and Treatment of Hypothyroidism: Failure to Demonstrate the Metabolic Insufficiency Syndrome (Controlled Study)**
S. H. Sikkema. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **20**, 546–555, April, 1960. 2 figs., 24 refs.

There is no general agreement concerning the existence of the so-called metabolic insufficiency syndrome in patients who complain of fatigue and often have symptoms compatible with a diagnosis of hypothyroidism. In some cases the serum protein-bound iodine (P.B.I.) level is normal although the basal metabolic rate (B.M.R.) is low. The condition is said to respond to administration of triiodothyronine but not to thyroid extract. A double-blind trial of triiodothyronine and a placebo was carried out in 20 students, seen in the Medical Clinic of the University of Minnesota Health Service, Minneapolis, whose chief complaint of fatigue did not appear to be adequately explained by the history or the results of physical examination and laboratory studies. No significant difference was observed between the results obtained with the drug and placebo, 11 patients benefiting from triiodothyronine and 10 from the placebo.

A group of 132 students with similar symptoms associated with a low B.M.R. and often with menstrual disturbances were given triiodothyronine in a dosage of 50 μg. daily, which was increased, if symptoms were not relieved, to a maximum of 150 μg. daily. In 75 (55%) there was convincing improvement following this treatment and these were considered to be suffering from hypothyroidism. The B.M.R. appeared to be of little value in predicting whether or not the patient would respond to treatment. The serum P.B.I. level was normal in the successfully-treated subjects and the author suggests that this value is of no help in the diagnosis of mild hypothyroidism. Triiodothyronine therapy was discontinued for 2 weeks in 17 of the hypothyroid students who had improved; all relapsed. Treatment was resumed with thyroid extract in equivalent doses, when the symptoms of fatigue were once more controlled.

The author found no evidence in this investigation to support the concept of the syndrome of metabolic insufficiency. *H.-J. B. Galbraith*

1241(a). **The Use of Radioactive Iodine in the Evaluation of Thyroid Nodules**
J. N. Attie. *Surgery* [*Surgery*] **47**, 611–614, April, 1960. 1 fig., 19 refs.

1241(b). **The Diagnosis of Thyroid Cancer with Radioactive Phosphorus**
N. B. Ackerman, D. B. Shahon, and J. F. Marvin. *Surgery* [*Surgery*] **47**, 615–622, April, 1960. 7 figs., 14 refs.

Writing from the Maimonides and Long Island Jewish Hospitals, New York, the author of the first of these papers reviews both the literature on, and his personal experience of, the value of radioactive iodine (^{131}I) in the differential diagnosis of thyroid "nodules". Between January, 1956, and June, 1959, of 148 patients with solitary or discrete thyroid nodules operated on, 107 had previously been given a test dose of ^{131}I and the thyroid gland mapped or scanned by means of a collimated Geiger–Müller or scintillation counter. The nodule was then classified as "cold, warm, or hot", according to its concentration of ^{131}I. It was concluded that 15 of 63 "cold" nodules, one of 28 "warm" nodules, and 2 of 16 "hot" nodules were malignant. The author suggests that these results show that thyroid scanning after administration of ^{131}I is useful in the diagnosis of thyroid cancer but is not always reliable. He operates on all "warm" and "cold" nodules, but only on "hot" nodules if they do not regress after treatment for 3 months with thyroid hormone.

The second paper, from the University of Minnesota, Minneapolis, describes the use of radioactive phosphorus (^{32}P) to diagnose the presence of thyroid cancer in 29 patients. In this method, 24 hours after an oral dose of a 0·5 mc. of ^{32}P the radioactivity in any suspicious area of the thyroid gland was compared with that in the remaining areas of the gland. The ratio of the count rate in the suspected area to that in the normal areas was found to be 0·93 in 6 patients not operated on, of whom 3 had a benign condition. In 14 histologically proved benign lesions and one well-differentiated follicular carcinoma the ratio ranged from 0·85 to 1·12 and from 1·33 to 1·61 in 6 patients of whom 5 had malignant lesions and one Hashimoto's thyroiditis. The authors suggest that a raised uptake of ^{32}P may indicate malignancy.

[It is interesting to read these two papers together. The first author finds the use of ^{131}I in the diagnosis of thyroid cancer fallible, while those of the second paper apply a ^{32}P-uptake test, as has also been done in nearly every other kind of accessible malignant disease, but do not find it noticeably better than ^{131}I. It is perhaps still true that histological examination is the only absolutely reliable method of diagnosing suspected malignant disease.] *K. E. Halnan*

PANCREAS

1242. Obesity and Diabetes: a Reëvaluation

S. K. FINEBERG. *Annals of Internal Medicine* [*Ann. intern. Med.*] **52**, 750–760, April, 1960. 20 refs.

The author briefly reviews previous work on the effect of weight reduction in the obese diabetic with mild, mature onset of the disease. He emphasizes that weight reduction has been accompanied not merely by a disappearance of hyperglycaemia but also, in many instances, by a return to normal of the response to the standard glucose tolerance test. A group of 80 grossly obese diabetic patients attending the Diabetic Clinic of the Harlem Hospital, New York, were given either 25 mg. of phenmetrazine hydrochloride (" preludin ") or a placebo. Neither the patient nor the physician responsible for supervising the treatment knew whether the patient was receiving the placebo or the active drug, and the patients themselves were not told of the object of the trial. Supervision was continued for a period of 4 months, the patients being seen monthly. No dietary instructions were given, but the majority of the patients were taking a diet containing 1,100 to 1,200 Calories.

Of the 80 patients 12 were withdrawn because of unsatisfactory cooperation, 9 because oedema developed and 5 on account of side-effects. Of the remaining 54, 29 had received phenmetrazine and 25 the placebo, the groups being comparable, for purposes of analysis, as regards sex, age, and mean age. In 27 of the 29 patients in the phenmetrazine group the loss of weight was significant, ranging from ½ lb. (227 g.) to 26¼ lb. (12 kg.); 20 of these lost at least ½ lb. a week throughout the period of the trial. Of the 25 patients given a placebo, 15 lost weight, but only 3 lost an average of ½ lb. a week during the trial. In half the patients taking insulin and phenmetrazine the insulin dosage could be reduced.

The author emphasizes the importance of weight reduction in the control of diabetes and the value of anorexogenic drugs; he suggests that the evidence from the trial indicates that the effect of phenmetrazine is pharmacological and not psychogenic. He also stresses the need for the control of obesity in the treatment of diabetes mellitus in order to prevent the misuse of the oral hypoglycaemic agents. *R. E. Tunbridge*

1243. Early Vascular Changes in Diabetes Mellitus

J. DITZEL, D. W. BEAVEN, and A. E. RENOLD. *Metabolism: Clinical and Experimental* [*Metabolism*] **9**, 400–407, April, 1960. 4 figs., 14 refs.

From the Peter Bent Brigham and New England Deaconess Hospitals (Harvard Medical School), Boston, are reported observations on the vascular bed in the conjunctivae of 56 young diabetic patients between the ages of 10 and 40 years and 50 non-diabetic healthy individuals. The studies established that in the diabetic there was a dilatation of the venules, which was greatest in the early morning and least in the middle afternoon, and that this dilatation tended to become irreversible in most diabetics in whom the disease was of more than 15 years' duration. A group of insulin-deprived diabetic patients showed a similar improvement during the day, from which the authors conclude that the dilatation is not related to insulin deficiency.

Infusions of ACTH (corticotrophin) effectively increased the endogenous corticosteroid secretion, but failed to aggravate the venular dilatation of the diabetic subjects. The authors discuss the nature of the dilatation, which at present is but poorly understood.

I. McLean Baird

1244. Some Observations on the Use of Chlorpropamide in Primary Tolbutamide-failure Diabetics

L. L. MORGENSTERN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **52**, 761–772, April, 1960. 6 figs., 8 refs.

The clinical and biochemical findings in 13 diabetic patients treated with chlorpropamide, including 12 who had previously failed to respond to tolbutamide, are described. Chlorpropamide was clinically effective in 6 patients, all of whom had shown no response to tolbutamide. The findings, however, reaffirmed that there is no sure way of predicting the success of treatment with chlorpropamide. There was no correlation between the blood level of the drug and the blood sugar level, although it appeared probable that the former should be at least 100 μg. per 100 ml. before a clinical response is obtained. The author suggests that a combination of chlorpropamide and insulin might be useful in certain cases. [There is no information concerning the benefits of long-term combined therapy.] In one case the daily dose of chlorpropamide was 1 g., a potentially toxic dose. Further, in brittle diabetics there was no evidence, even short-term, of the benefits of combined therapy. *R. E. Tunbridge*

1245. Response to Glucagon by Subjects with Hyperinsulinism from Islet-cell Tumours

V. MARKS. *British Medical Journal* [*Brit. med. J.*] **1**, 1539–1540, May 21, 1960. 1 fig., 9 refs.

At the National Hospital, Queen Square, London, glucagon, the hyperglycaemic–glycogenolytic factor which, it is generally agreed, works in conjunction with insulin to facilitate the transport of glucose from the liver to the peripheral tissues and its utilization there, was administered to 4 subjects with organic hypoglycaemia due to hyperinsulinism. The 1-mg. dose was given by intramuscular injection some 6 to 8 hours after the last meal. Two of the patients investigated had a blood sugar level below 40 mg. per 100 ml. before the glucagon injection, but only one displayed symptoms of hypoglycaemia. In all 4 subjects the injection was followed by a rapid rise in the blood sugar level, which was maximum at the 30th minute and fell to the lower limit of normal or lower by the 90th minute. At the end of 2 hours all 4 patients were hypoglycaemic and 2 showed severe symptoms necessitating treatment. This hypoglycaemic phase following a normal rise in blood sugar thus distinguishes the response of patients with hyperinsulinism from that observed in healthy subjects. It is suggested that the glucagon test may be useful in the differential diagnosis of the hypoglycaemic syndrome and of hyperinsulinism from islet-cell tumours.

A. I. Suchett-Kaye

The Rheumatic Diseases

CHRONIC RHEUMATISM

1246. **Radiological and Clinical Investigation of the Temporo-maxillary Joint. Application to the Study of Temporo-maxillary Arthritis in the Course of Chronic Inflammatory Rheumatism (Rheumatoid Arthritis and Ankylosing Spondylitis).** (Exploration radioclinique de l'articulation temporo-maxillaire. Application à l'étude des arthrites temporo-maxillaires au cours des rhumatismes inflammatoires chroniques (polyarthrite chronique évolutive et spondylarthrite ankylosante))
P. MÉRIEL, R. RUFFIÉ, H. CADENAT, A. FOURNIÉ, and P. BLANC. *Journal de radiologie, d'électrologie et de médecine nucléaire* [*J. Radiol. Electrol.*] **41**, 105–118, March–April, 1960. 24 figs., 20 refs.

Writing from the Centre de Rhumatologie, Toulouse, the authors first describe the anatomy of the temporo-mandibular joint, recalling that the condyle of the mandible has two convex surfaces separated by a crest. The whole condyle is intra-articular, but only the anterior aspect is covered with cartilage. The joint, which is a very complex structure, is in relation with the external auditory canal behind and with the chorda tympani, auriculo-temporal nerve, and sympathetic fibres. A biconcave meniscus articulates with the convex upper surface of the mandibular condyle below and the temporal condyle of the zygoma above, thus in effect dividing the joint into two synovial cavities. The movement of the joint is also complicated. In opening the mouth there is first a very slight rotation of the mandibular condyle about its transverse axis and then a forward and downward movement of the temporal condyle; the structure of the joint also allows for free lateral and antero-posterior movements. The articulation of the lower jaw is based partly on the temporo-mandibular joint, but also partly on the articulation with the maxilla along the line of dental closure.

In chronic rheumatism involvement of the joint may give rise to pain in the region of the ear. This pain, which is worse in the morning when the subject first moves his lower jaw, may be unilateral or bilateral and is aggravated by use of the joint in speaking, mastication, or swallowing; indeed the limitation in movement of the mandible and the desire to avoid the pain may eventually interfere with nutrition. Since the joint is overshadowed by the dense bone formations of the skull, radiology is difficult and requires careful interpretation. The radiograph is taken in profile by siting the x-ray tube at the sigmoid notch of the opposite mandible with the mouth widely open and the cassette parallel to the sagittal plane in contact with the ear on the affected side. The principal rays will therefore be directed upwards and slightly backwards. An antero-posterior exposure is obtained by placing the tube as near the upper and outer angle of the orbit as possible with the mouth open and with the cassette behind the skull, perpendicular to the incident rays. (The method is portrayed in diagrams.) A total of 40 cases, comprising 35 cases of adult and 5 of juvenile rheumatoid arthritis, were studied by the authors. In 21 cases (52%) there were some subjective symptoms and 14 had some limitation of movement at the joint, while clinical signs of involvement of the temporo-mandibular joint were noted in 33 (82%) of cases. Radiology revealed lesions in 37% and in 27% there were both clinical and radiological signs. Lesions of the mandibular condyle included erosions of varying extent and depth, cyst formation, osteosclerosis, and atrophy, while calcification of the meniscus was demonstrated in 2 cases. In one case of juvenile rheumatoid arthritis agenesis of the mandibular condyle and a persistent concavity of the lower border of the mandible were discovered.

Discussing the aims of treatment the authors stress the importance of securing good occlusion in the dental articulation and point out that for this free movement at the joint is necessary. In acute exacerbations they recommend resting of the joint, together with a liquid diet and enforced silence. For local treatment they advocate injections of hydrocortisone.

William Hughes

1247 (a). **Choline Salicylate: a New, Effective, and Well-tolerated Analgesic, Anti-inflammatory, and Antipyretic Agent**
R. H. BROH-KAHN. *International Record of Medicine* [*Int. Rec. Med.*] **173**, 217–233, April, 1960. 4 figs., 30 refs.

1247 (b). **Observations on the Usefulness of a New Liquid Salicylate in Arthritis**
D. NEVINNY and J. D. C. GOWANS. *International Record of Medicine* [*Int. Rec. Med.*] **173**, 242–247, April, 1960. 14 refs.

1247 (c). **Comparative Evaluation of the Effectiveness of Choline Salicylate in Treatment of Arthritis and Allied Conditions**
R. P. THOMAS JR. *International Record of Medicine* [*Int. Rec. Med.*] **173**, 248–254, April, 1960. 10 refs.

These three papers form part of an American symposium on a new and highly soluble salicylate preparation, the choline salt of salicylic acid ("arthropan"), which appears to represent an advance over previous forms of salicylate therapy. This new agent is given in liquid form in a cherry-flavoured vehicle in a dose of 1 to 2 teaspoonfuls (5 to 10 ml.), each teaspoonful containing 870 mg. of choline salicylate, that is, the equivalent of 500 mg. of salicylate or 10 grains (650 mg.) of aspirin. Tests showed that it is absorbed about five times more rapidly than aspirin and provides peak plasma salicylate levels within 10 minutes, as compared with

120 minutes for aspirin; also several doses may be given each day. All three papers comment on the effective analgesic, anti-inflammatory, and antipyretic actions of the new preparation, on its ease of administration, on the relative lack of gastro-intestinal irritation, and on the fact that patients who cannot tolerate aspirin are able to take choline salicylate.

The author of the first paper, from New York City Department of Health, supervised a long-term cooperative trial of the drug carried out by 80 physicians on 1,200 patients, in many of whom cross-over studies were performed in order to compare it with aspirin. The authors of the second paper, who report from Tufts University School of Medicine, Boston, gave the drug to patients with rheumatoid arthritis, 20 being treated on a short-term basis and 30 receiving long-term maintenance therapy. The third paper, from the Nix Memorial Hospital, San Antonio, Texas, also describes the treatment of 45 patients with arthritis. The authors are unanimous in concluding that choline salicylate is a salicylate of choice for all patients with chronic arthritis and the salicylate of choice for the many who are intolerant of other forms of salicylate. *T. B. Begg*

1248. **Steroid Arthropathy of the Hip**
D. R. Sweetnam, R. M. Mason, and R. O. Murray. *British Medical Journal* [*Brit. med. J.*] **1**, 1392–1394, May 7, 1960. 7 figs., 8 refs.

The authors describe 4 patients who, while under treatment at the London Hospital during which they received relatively high doses of steroids, developed severe damage to their hip-joints with rapid destruction of the femoral head. The fact that these changes, once they started, were comparatively rapid and painless, led the authors to suppose that it might have been the steroids which were responsible [although they advance no very convincing reason for this belief]. They agree that even in the absence of steroid therapy severe destruction can occur in these joints in arthritic patients, but point out that then the joint changes are more gradual, less extensive, and pain is a prominent feature.

In discussing causation they suggest that the relief given by steroid therapy may encourage patients to subject damaged joints to over-use, and so precipitate a stage of disorganization which would otherwise have been delayed or might even not have occurred. It is urged that patients on high-dosage steroid therapy should be carefully observed for signs of destruction of the hip-joint. *W. S. C. Copeman*

1249. **Neuropathy in Rheumatoid Disease**
V. L. Steinberg. *British Medical Journal* [*Brit. med. J.*] **1**, 1600–1603, May 28, 1960. 19 refs.

From the London Hospital are described 18 cases in which neurological lesions occurred during the course of rheumatoid arthritis. Although the condition seems to have been originally described by French workers in 1887, there has recently been an increase in the number of these cases, perhaps coinciding with the introduction of steroid therapy. The condition is equally distributed between the sexes although rheumatoid arthritis is at least twice as common in women as in men. Of the present series 5 patients died, all within a year of onset of this complication, 3 of them within one month. The prognosis when neurological lesions develop in rheumatoid arthritis must thus be considered to be serious.

The lower limbs only were involved in 12 cases, the arms only in one, and both upper and lower limbs in 5. The symptoms were mainly a sensation of tingling, burning, and numbness of the extremities, but muscle pain was also often present with tenderness of the calves; in all cases objective sensory loss to light touch, pinprick, and temperature was found. The deep reflexes were generally preserved, except for the ankle jerks in 7 cases. There was motor weakness in some cases, accompanied by foot-drop in 6. In 10 of the cases there appeared to be some connexion between the onset of this complication and steroid therapy which had either just been started, or recently stopped, or the dosage of steroids drastically reduced. The complication was not affected by any form of treatment. L.E. cells had been detected in the serum of 3 male patients at one time or another. There was post-mortem evidence of arteritis in the peripheral nerves in 2 cases, and it is considered that this may be the cause of the neuropathy. *G. S. Crockett*

1250. **Rheumatoid Neuropathy**
F. D. Hart and J. R. Golding. *British Medical Journal* [*Brit. med. J.*] **1**, 1594–1600, May 28, 1960. 25 refs.

Writing from Westminster Hospital, London, the authors discuss 42 cases of rheumatoid neuropathy as seen in 18 men and 24 women ranging in age from 36 to 88 years, the majority being aged between 40 and 60. In 15 of these cases no steroids had been administered within 3 years of the onset of the neuropathy, and 12 had received no steroids at all. A further 20 however had regularly received steroids and in 6 there had been a recent sudden withdrawal of this treatment.

In 13 cases the onset of the condition was abrupt, with numbness and " deadness " in the toes and feet or intolerable burning pain, but in the others it was more gradual and insidious. The complaint was usually bilateral and symmetrical. Sensory changes were considerable and affected all modalities, but sense of position usually remained well preserved. Although there was muscle wasting and loss of power in many cases, in only 8 was the ankle reflex absent bilaterally. In 2 cases there was transient facial hypo-aesthesia at the time of development of the neuropathy. The presence of L.E. cells was established in only 4 patients. The serum vitamin B_{12} level was found to be normal in the 9 cases in which it was assayed. In regard to outcome, of the 42 cases 20 have remained unchanged, 14 have improved, 2 patients have died, 5 have apparently recovered, and one runs a fluctuating course. No treatment seems to be effective. Vascular necrotic lesions of the fingers occurring during the course of this condition constitute a bad prognostic sign. In 5 patients examined at necropsy, in all of whom " steroid therapy clearly contributed to the general condition and downhill course ", diffuse arteriopathy with arteritis of the vasa nervorum

was found and this, at least at present, is generally accepted as the probable explanation of the condition, though it does not explain adequately all cases.

G. S. Crockett

1251. **Erythrocyte Survival in Rheumatoid Arthritis**
S. M. Lewis and I. H. Porter. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **19**, 54–58, March [received May], 1960. 2 figs., 9 refs.

In this paper from the Postgraduate Medical School of London the authors describe a study of erythrocyte survival in 50 patients with rheumatoid arthritis. The patients' erythrocytes were labelled with radioactive chromium (^{51}Cr) by the method of Mollison and Veall (*Brit. J. Haemat.*, 1955, **1**, 62) and then re-injected. Venous blood samples were collected at regular intervals and the radioactivity compared with that found in a similar study in 20 normal men and women. The results were corrected for decay but not for elution of chromium from intact erythrocytes.

In 46 of the rheumatoid patients the ^{51}Cr activity was within the normal range. In the remaining 4 there was a slight increase in the rate of cell elimination due to the early loss of about 15% of the labelled cells, the reason for which was unknown. Gastro-intestinal blood loss was estimated by measuring the radioactivity of the stools after the labelling process. Some haemorrhage occurred in all but one of the patients, but the blood loss was not sufficient to have influenced the rate of elimination of labelled cells. The authors conclude that haemolysis is not a feature of rheumatoid arthritis and does not account for the anaemia so often seen in this condition.

K. C. Robinson

1252. **Importance of Aspirin as a Cause of Anaemia and Peptic Ulcer in Rheumatoid Arthritis**
F. D. Baragar and J. J. R. Duthie. *British Medical Journal* [*Brit. med. J.*] **1**, 1106–1108, April 9, 1960. 21 refs.

The case records were studied of 244 patients admitted to the Rheumatic Diseases Unit, Northern General Hospital, Edinburgh, with rheumatoid arthritis, most of whom had been taking aspirin continuously or intermittently in varying dosages for a number of years. The haemoglobin level was determined on admission, on discharge, and approximately at 2, 4, and 6 years thereafter. A more detailed study was made of those cases in which the haemoglobin level was significantly low. Although the majority of the patients were taking aspirin regularly, the exact dosage was not always known. The authors therefore selected 75 patients who were taking a minimum of 40 gr. (2·6 g.) and usually 60 gr. (3·9 g.) of aspirin a day, and compared their progress with that of 31 patients who did not receive salicylates or only very occasionally.

Over the 6-year period there was a significant increase in the haemoglobin level in the patients receiving salicylates, which was directly comparable with the increase observed in the smaller group not taking aspirin regularly. Although of all patients 30 (12·3%) complained of dyspepsia there was clinical or radiological evidence of peptic ulceration in only 10 (4%). At the final assessment the haemoglobin level in 27 (11%) patients was below 80% (100% equal to 14·8 g. per 100 ml.), but only in 3 of these was there evidence of peptic ulceration. Although in 12 cases other diseases were present which might possibly have had a bearing on the anaemia, it is considered that the cause of the anaemia in the majority of patients was active rheumatoid arthritis.

A review of the literature revealed that the incidence of peptic ulceration in this series compared favourably with that in the general population. It is concluded that regular aspirin can be tolerated for long periods by patients with rheumatoid arthritis, without any increase in anaemia, and that the risk of intra-intestinal haemorrhage or peptic ulceration resulting from salicylate therapy has probably been exaggerated.

J. Warwick Buckler

COLLAGEN DISEASES

1253. **Treatment of Polyarteritis Nodosa with Cortisone: Results after Three Years**
Report to the Medical Research Council by the Collagen Diseases and Hypersensitivity Panel. *British Medical Journal* [*Brit. med. J.*] **1**, 1399–1400, May 7, 1960. 1 ref.

An earlier report to the Medical Research Council on this subject (*Brit. med. J.*, 1957, **1**, 608; *Abstr. Wld Med.*, 1957, **22**, 133) presented the results of one year's cortisone therapy in 17 patients with polyarteritis nodosa. These were compared, retrospectively, with an untreated group which came under medical care before the days of cortisone treatment. These two groups, however, differed in one important respect, namely, a difference in the incidence of hypertension; this was significantly higher in the untreated group and is important in that it adversely affects the prognosis in this disease.

The present report includes 4 further treated cases, making a total of 21 biopsy-proved cases which have now been observed for a minimum of 3 years from the beginning of cortisone treatment. Of these 21 patients there were 13 survivors at 3 years, but 3 of these died, 2 in the 4th and one in the 5th year. Of the 19 untreated patients 12 (63%) died within 9 months of biopsy, whereas 18 (86%) of the treated patients were then still alive. It is essential to note, however, that the untreated group initially included 8 patients with hypertension all of whom died within one year, whereas at the start of the study there was only one hypertensive patient in the treatment group, although 9 others in this group developed hypertension during the course of the trial. At the end of 3 years 13 (62%) of the treated group, as compared with 7 (37%) of the untreated, were alive. This apparent advantage disappears, however, when patients with hypertension are excluded.

The report lays stress on the limitations of this trial, which arose from the unjustifiability of having a concurrent untreated control group. At the start of treatment there was speedy and often dramatic improvement

in most patients, but later unpleasant and serious complications developed in a few. The trial has not produced evidence that cortisone, in the dosage given to these patients, improved the chances of ultimate recovery, although it may possibly have postponed death.

G. Loewi

1254. "Delayed" Cutaneous Hypersensitivity to Leukocytes in Disseminated Lupus Erythematosus

E. A. FRIEDMAN, W. A. BARDAWIL, J. P. MERRILL, and C. HANAU. *New England Journal of Medicine* [*New Engl. J. Med.*] **262**, 486–491, March 10, 1960. 4 figs., 18 refs.

The incidence of delayed cutaneous reactions to intradermal injection of leucocytes in disseminated lupus erythematosus (D.L.E.) was studied in a number of patients at four hospitals in Greater Boston, Massachusetts. Suspensions of leucocytes from patients and donors were prepared by centrifuging plasma after sedimenting out the erythrocytes of freshly drawn blood in heparin and dextran at 4° C. for up to one hour. The leucocytes were resuspended in plasma to a concentration of 30,000 to 90,000 per c.mm. and a dose of 0·1 ml. was injected intradermally. Control injections containing dextran in plasma, dextran solution, or erythrocytes gave negative reactions.

Positive skin reactions to both autologous and donor leucocytes were obtained in 16 out of 20 patients with D.L.E., 2 out of 7 with typical rheumatoid arthritis (both of whom gave a positive response for the antinuclear factor by the fluorescent antibody technique), and in only one, with osteoarthritis, out of 51 controls with various diseases. Of the 4 non-reactors with D.L.E. 3 were taking at least 20 mg. of prednisolone daily. Positive reactions were of the delayed type, maximal at 24 hours, indicating either reactions with fixed cellular antibody or, more simply, the time taken for the inoculated leucocytes to break down and release intranuclear materials able to react as antigens with circulating antibodies. Microscopically the positive reaction differed from the negative reaction in showing accumulations of host cells, mainly polymorphonuclear leucocytes, in the deep dermis and subjacent fat and changes in the overlying epidermal cells. The authors caution against interpreting this reaction as explaining the pathogenesis of D.L.E. or its associated leucopenia.

Allan St. J. Dixon

1255. Diagnosis of Polymyositis

K. W. G. HEATHFIELD and J. R. B. WILLIAMS. *Lancet* [*Lancet*] **1**, 1157–1161, May 28, 1960. 4 figs., 22 refs.

The authors present from St. Bartholomew's Hospital, London, and Lister Hospital, Hitchin, Herts, a study of 28 cases of polymyositis. In this disorder diagnosis may be difficult, since muscle biopsy may give only normal results, the electrical findings may be misleading, and the clinical picture atypical; fortunately, however, 2 of these 3 features are usually positive. The rapid onset of muscular weakness, the occurrence of spontaneous remission, or the elicitation of brisk reflexes at a stage when these would be absent in true muscular dystrophy tend to differentiate the latter condition from myositis. In 3 of the authors' patients there was spontaneous fasciculation, with wasting of the tongue. Differentiation from motor-neurone disease is made more difficult by electromyography (EMG), which often shows high-voltage potentials suggesting involvement of anterior-horn cells. One of these patients responded to neostigmine. In considering the collagen diseases it is noted that although skin changes predominate in scleroderma, muscular weakness and wasting are also common. Another possible cause of myopathy is sarcoidosis, and thyrotoxic myopathy must also not be overlooked. In polyarteritis nodosa, the peripheral neuropathy and sensory changes usually underlie the muscular weakness. In 5 of the present cases there was an association between dermatomyositis (and polymyositis) and carcinoma. Of the 28 cases an abnormal finding on muscle biopsy was obtained in 26.

Typically, there is a myopathic EMG pattern, together with evidence of partial denervation. The latter is shown by the EMG (fibrillation potentials), or by the abnormal strength–duration curves. Partial denervation, which distinguishes polymyositis sharply from the chronic muscular dystrophies, was present in all but 2 of the cases. Other pathological investigations are not of great help and in doubtful cases it may be justifiable to use steroids as a therapeutic test.

D. Preiskel

ACUTE RHEUMATISM

1256. Epidemic Cervical Myalgia

D. M. DAVIES. *Lancet* [*Lancet*] **1**, 1275–1277, June 11, 1960. 8 refs.

In the autumn of 1958 and again in the late summer of 1959 a small epidemic of acute myalgia affecting the trapezius muscles occurred among nurses at the London Hospital, 13 nurses reporting sick out of a total staff of about 725; probably many others were affected to a milder degree and did not seek medical advice. All except one of the 13 nurses were admitted as patients. The chief symptom was acute pain and tenderness of the trapezius muscles, although this did not necessarily occur at the start of the illness; 10 of the patients also complained of mild transient aches in various other muscles and in joints. In some cases there was slight fever for a day or two. The illness, which lasted for an average of 9 days, was not accompanied by any inflammation of the throat or by enlarged glands. The leucocyte count was normal in most cases and the results of the Paul–Bunnell test were negative. The erythrocyte sedimentation rate was raised in only 2 of the 10 cases in which this was estimated. A virus infection was suspected as the cause of this illness, but attempts to identify various viruses by examination of stools or by agglutination or complement-fixation reactions failed.

The author considers that the clinical picture was distinct from that of Bornholm disease and the results of the virological investigations did not support a diagnosis of the latter. Epidemics of acute cervical pain of a very similar character have been described previously.

B. E. W. Mace

1257. **Benign Polyarthritis**
J. S. LAWRENCE and P. H. BENNETT. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **19**, 20–30, March [received May], 1960. 3 figs., 23 refs.

The results of a survey of rheumatic disease in a random sample of the population (subjects aged 15 years and over) in the town of Leigh, Lancs., are reported in this paper from the Empire Rheumatism Council Field Unit, University of Manchester. A history of all symptoms, whether rheumatic or not, was taken, the skeletal system was examined in detail, and blood pressure was recorded. In 34 (5%) of 653 males and 50 (7%) of 690 females there had been one or more episodes of a form of polyarthritis. It occurred most frequently in the winter months, with first episode usually between the ages of 5 and 24 years; they were seldom admitted to hospital. Of the 84 subjects giving such a history only 4 had definite evidence of rheumatic heart disease, but 23 had joint residua (excluding osteoarthritis). These changes included subluxation in the interphalangeal and metatarso-phalangeal joints and pain or stiffness in the metacarpo-phalangeal joints, wrists, knees, tarsal joints, and cervical spine. Radiologically, changes were observed particularly in the cervical spine. The sheep cell agglutination test was carried out in all cases but the reaction was positive in only 7%. The authors discuss the aetiology of this benign form of polyarthritis. *K. C. Robinson*

1258. **The Concept of Egg Yolk as a Dietary Inhibitor to Rheumatic Susceptibility**
A. F. COBURN. *Lancet* [*Lancet*] **1**, 867–870. April 16, 1960. 23 refs.

It is now accepted that the haemolytic streptococcus is the infective agent in rheumatic fever, but the factors which determine rheumatic susceptibility are uncertain. After the Second World War, in one area in Chicago where there was an increased food consumption associated with a rise in family income, a marked decline in the incidence of rheumatic fever was noted, in spite of the occurrence of the expected number of Group-A streptococcal infections. This fall, however, was not observed among the negro population in a nearby neighbourhood, whose family incomes remained extremely low.

Analysis of information concerning diet obtained from the replies to a questionary suggested the possibility of an association between poverty and low consumption of egg-yolks by children in whom rheumatic disease developed. Small groups of rheumatic children were therefore given supplements of egg-yolk or fractions of egg-yolk in their diet. It was found that the incidence of recurrence of rheumatic fever after streptococcal infection fell below that anticipated. The author states that an anti-allergic component has been isolated from egg-yolk; this is an alcohol-soluble substance and protects animals against immediate and delayed types of hypersensitivity.

It is concluded that since the underlying biochemical mechanism of the rheumatic state is not known its relation to nutrition in infancy remains to be determined. *B. M. Ansell*

1259. **The Prophylaxis of Rheumatism with "Iversal".** (Rheumatismus-prophylaxe mit Iversal)
K. LORENZ. *Monatsschrift für Kinderheilkunde* [*Mschr. Kinderheilk.*] **108**, 268–270, May, 1960. 11 refs.

Because side-effects are apt to occur during continuous prophylaxis with both sulphonamides and penicillin in children who have had an attack of rheumatic fever, other forms of chemoprophylaxis may be tried. For this purpose the author, working at the Children's Hospital, Dresden, has used "iversal", a compound synthesized in 1955 by Domagk and Petersen, of which the chemical composition is benzochinon-guanylhydrazone-thiosemicarbazone. It is highly effective locally against streptococci in dilutions of up to $1:10^6$, but even this concentration cannot be obtained in the bloodstream after systemic administration without causing toxic side-effects. The drug is normally dispensed in chocolate-flavoured tablets containing 10 mg. of the active substance, these being given 4 or 5 times daily and allowed to disintegrate slowly in the mouth—they must not be chewed or swallowed. Used in this way they cause no toxic side-effects and are well tolerated by children for a short time, but after some weeks the taste becomes unpalatable and there is also a definite loss of appetite. The author found that better tolerance was achieved when the tablets were flavoured with peppermint.

Altogether 45 rheumatic children have been treated for a total of 16 patient-years [that is, the average duration was only about 4 months] and during this time no recurrences of rheumatic fever were observed. Nevertheless, haemolytic streptococci were recovered on throat swabbing from 10 children on 17 occasions. There was no concurrent sore throat or a rise in the antistreptolysin-O titre. These children were considered to be carriers of the streptococci. Prophylaxis with iversal is thought to be particularly valuable in children who are sensitive to penicillin. *John Lorber*

1260. **Acute Benign Pericarditis and Acute Articular Rheumatism in Children** (Péricardite aiguë bénigne et rhumatisme articulaire aigu chez l'enfant)
R. A. MARQUEZY and C. BACH. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **36**, 1206–1211, April 24, 1960. 16 refs.

Acute benign pericarditis in adults is not uncommon but in children appears to be rare, the authors having found only 29 cases reported in the literature. In this paper they describe 3 cases of pericarditis in children, not due to rheumatism, seen at the Hôpital Trousseau, Paris, between 1948 and 1957, and contrast the findings with those in a similar case of rheumatic origin.

The first patient was a boy of 13 who had 6 separate attacks of pericarditis in one year, the signs being pain, fever, and pericardial friction; on each occasion these responded to administration of steroids but later recurred. There was no acute joint involvement or cardiac valvular lesion during the year of illness nor in 3½ years of follow-up. The second patient, a boy aged 7, had a single attack of pericarditis associated with a pulmonary infection which responded to penicillin. The third, a boy aged 11, had a single attack of pericarditis with shoulder

pain which responded to ACTH; no recurrence and no cardiac lesion was found in 5 years of follow-up. No specific cause was found in any of these 3 cases, and their subsequent course appeared to exclude rheumatism.

The contrasting case was in a girl aged 13 who had 7 attacks of pericarditis in one year, these responding to steroids each time but relapsing after cessation of treatment. From the start she had a pansystolic murmur, and the 5th attack of pericarditis was associated with joint symptoms, making the clinical diagnosis of rheumatism probable. Nevertheless the heart murmur subsequently disappeared, leaving her with an apparently normal heart. *J. A. Cosh*

1261. **A Comparison of the Effect of Prednisone and Acetylsalicylic Acid on the Incidence of Residual Rheumatic Heart Disease**

COMBINED RHEUMATIC FEVER STUDY GROUP. *New England Journal of Medicine* [*New Engl. J. Med.*] **262**, 895–902, May 5, 1960. 11 refs.

Of the 8 hospitals which took part in the Combined Rheumatic Fever Study Group set up in 1956 to compare the effects of prednisone and aspirin in the treatment of rheumatic heart disease in children, 4 were in New York City, 2 in Baltimore, one in Boston, and one in Cleveland, Ohio. In this paper the investigators report on the results of a carefully controlled study of 57 patients who were all aged 12 years or under and in whom the attack of rheumatic carditis was the first one and had not been present for more than 28 days. The other stringent criteria for admission to the trial were the presence of one or more of the following signs: a pericardial friction rub or effusion, unequivocal cardiac enlargement confirmed radiographically, congestive cardiac failure, and a significant aortic or apical diastolic murmur or a Grade-3 apical systolic murmur; a Grade-2 apical systolic murmur was accepted only if a diastolic murmur or other stigmata of carditis were present. Patients were assigned to one of two treatment groups by random selection: Group 1 received prednisone in a dosage of 60 mg. daily for 3 weeks in divided doses, this being then gradually reduced over the subsequent 9 weeks until a total of 3 g. had been given; Group 2 was given acetylsalicylic acid in a dosage of 50 mg. per lb. (110 mg. per kg.) body weight daily in divided doses for 9 weeks, followed by 30 mg. per lb. (66 mg. per kg.) daily in divided doses for 2 weeks and then 15 mg. per lb. (33 mg. per kg.) daily for one week, this dosage being aimed at maintaining a serum salicylate level of between 25 and 35 mg. per 100 ml. For the eradication of Group-A streptococci both treatment groups received penicillin in doses sufficient to maintain therapeutic levels for 10 days and this was followed by long-term prophylaxis with one of the currently accepted prophylactic regimens. For the purposes of the trial the clinical and laboratory findings in each patient were recorded on admission, then after 12 weeks' therapy plus 3 weeks' observation, and finally one year after the completion of the therapy and observation periods.

Both prednisone and salicylates suppressed the inflammatory reaction caused by acute rheumatism, but no superiority was found in the group receiving prednisone as compared with that receiving salicylates. Even though clinical and other objective manifestations of the acute disease were well controlled, cardiac damage was not prevented. Although none of the 28 patients receiving these large doses of prednisone suffered any serious untoward reaction, the investigators consider that in view of the lack of significant reduction in residual heart damage such high dosage of steroids is unwarranted. *J. Warwick Buckler*

1262. **Prevention of Recurrent Rheumatic Fever in Children and Adults with Oral and Repository Penicillin**

T. W. MOU, H. A. FELDMAN, and H. HARTENSTEIN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **239**, 403–416, April, 1960. 2 figs., 23 refs.

The authors of this paper from the Departments of Preventive Medicine and Pediatrics, State University of New York, describe their experience at a rheumatic-fever prophylaxis clinic, where during the first 3 years of its existence 139 patients were observed for a total of 1,978 patient-months. The ages of the patients (55 male and 84 female) ranged from 8 to 74 years, only 39 being under 20 years. Once a month throat swabs were taken for culture and blood samples for estimation of the erythrocyte sedimentation rate, the haematocrit and C-reactive protein values, and the antistreptolysin-O titre. Alternate patients were assigned to one of two groups, the first group receiving 200,000 units of benzathine benzylpenicillin in tablet form once daily and those in the second group receiving 900,000 units of benzathine benzylpenicillin intramuscularly once a month. Patients with a history of penicillin hypersensitivity or who developed such hypersensitivity were given 0·5 g. of sulphamethoxypyridazine daily.

No recurrences of acute rheumatic fever were encountered during the period of observation. Discomfort or pain in the joints was reported at some time by 59 (42%) of the patients—slightly more frequently by those receiving penicillin intramuscularly than by patients given penicillin by mouth. The incidence of sore throat and other upper respiratory tract infections was about the same in the two groups (difference within 1%). Auscultation of the heart revealed no change during the observation period in 109 patients, fewer murmurs in 13 patients, and more murmurs in 7; in 10 patients the findings by auscultation were unreliable throughout. Group-A streptococci were isolated three times, Group-B streptococci three times, and Group-C streptococci twice. An increase in the antistreptolysin-O titre was noted in 23 patients (13 oral penicillin, 10 intramuscular), who had failed to receive penicillin for a month or more. Among patients receiving penicillin regularly a significant rise in antistreptolysin-O titre was noted in 30 given intramuscular injections and in 22 given the antibiotic by mouth. When the data on antistreptolysin-O titres for both groups were combined a progressive fall in the median titre was noted during the period of observation, although new patients were added as they were admitted to the clinic. Few allergic reactions were seen, and these were of little consequence apart from one episode of anaphylaxis following an initial injection. *C. E. Quin*

Neurology and Neurosurgery

1263. **Further Experiences with Intrathecal and Subdural Phenol: Observations on Two Forms of Pain**
R. M. MAHER. *Lancet* [*Lancet*] **1**, 895–899, April 23, 1960. 4 figs., 15 refs.

Pointing out that previous workers have demonstrated that pain produced externally is conducted by large A nerve fibres with a high conduction rate (30 to 100 metres per second) and by small C nerve fibres with a low conduction rate (0·3 to 1·6 metres per second), the author recalls that the first needs a greater stimulus to evoke pain than does the second and that duration of the pain is less; the first may be regarded as an " emergency " pain and the second as a " reminder " pain at the site of injury. The author has found that these principles also hold in regard to pain originating internally, as has been demonstrated by the intrathecal injection of phenol to cover the appropriate spinal root areas.

In the study here reported from the Pain Relief Centre, Manchester Regional Hospital Board, intrathecal phenol gave complete relief from pain in the lumbosacral region and dorsal regions below D3 in 61 out of 81 cases. Using a dose-gradation technique, relief was obtained in 12 out of 14 cases. For lesions above D3 intrathecal phenol was not used. If phenol alone proves ineffective silver nitrate may be added. The author noted that when pain is abolished patients seemed to live longer and spinal repair was sufficient sometimes for some months' walking. In cases of breast cancer perhaps irradiation and androgens had more time to act. It is pointed out that sensory and root reactions to phenol are greater in patients with non-malignant states, so that preliminary skin testing of the reaction to phenol is important. The method has been employed chiefly in malignant conditions, but cases of spasticity with flexor spasms, Parkinsonism, arthritis, spondylitis, failed disk operations, and disseminated sclerosis have also been treated.

[The original paper should be consulted for details of the technique, which varies with the nature of the disease and the site of the pain.] *G. de M. Rudolf*

1264. **Spinal Cord Syndromes Due to Vascular Conditions.** (Über gefässbedingte Rückenmarkssyndrome)
G. WOLF. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete* [*Fortschr. Neurol. Psychiat.*] **28**, 273–284, May, 1960. 1 fig., 34 refs.

From the University Neurological Clinic, Cologne, the author describes 3 patients who manifested all the signs of transverse section of the spinal cord which were shown to be due to disturbance in blood supply to the cord caused by occlusion of the intercostal and lumbar arteries at their point of departure from the aorta. For these cases the name of " syndrome of the middle and lower root arteries " is suggested. Clinically the signs consist in a sudden paralysis, as in transverse section of the cord, with complete sensory loss and simultaneous aortic disease. This syndrome is compared and contrasted with the " syndrome of anterior spinal artery occlusion ", which, however, shows dissociated sensory impairment. *J. Hoenig*

1265. **A Study of the Treatment of Sciatica.** (Enquête sur le traitement des sciatiques)
F. COSTE, R. WEISSENBACH, and G. ILLOUZ. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **36**, 1014–1024, April 4, 1960. 6 figs.

The authors review and discuss the current treatment of sciatica and point out that the " discovery " of prolapsed disk has not answered all the questions that arise in aetiology and treatment. They comment that patients recover from sciatica after receiving treatment which could not possibly influence herniation of an intervertebral disk, and conclude that the natural history of sciatica has yet to be written.

In an attempt to define more exactly the indications for the various forms of treatment commonly used for this disorder the authors have compared the therapeutic effects of anti-inflammatory drugs (phenylbutazone and hydrocortisone), epidural injections of procaine and steroids, subarachnoid injections of hydrocortisone or prednisone, spinal traction, swimming exercises, surgical intervention, and a placebo in 243 patients admitted to the Hôpital Cochin, Paris. Of 35 given the placebo only there was improvement in 46% and no change in 54% of cases. Of 38 given anti-inflammatory drugs there was improvement in 42% and no benefit in 58%. Surgical intervention produced moderate improvement in 29%, good to excellent results in 64%, and deterioration in 6%. With balneotherapy there was moderate improvement in 22%, good to excellent results in 49%, no change in 18%, and deterioration in 11%. Epidural injections produced some degree of improvement in 60%, and spinal traction in 53%, with deterioration in a small percentage or no change in the remainder. The results of traction of the spine were then studied in 444 ambulatory out-patients. It was found that the simultaneous administration of drugs made little difference to the results in this group, while the presence or absence of arthrosis made no difference. On the whole the results were better among those who stayed at home than among those who continued to work. These results were difficult to interpret, however, since the absence from work might have been determined either by the nature of the employment or the severity of the disease. The shorter the duration of the disease, the better were the results.

In general the authors consider that the value of rest in all forms of the disease is well proven. The acute painful forms, in which the patient finds it difficult or impossible to get into a position of rest, are suitable for epidural or intrathecal injections of procaine with hydro-

cortisone. Subacute or chronic cases respond well to spinal traction. For the relapsing case the authors advocate balneotherapy and the wearing of a corset. For cases with paralysis they advise surgical intervention.

William Hughes

DIAGNOSTIC METHODS

1266. **The Electroencephalogram in Cerebellar or Tonic Fits**

R. R. J. Strobos and E. Alexander Jr. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **12**, 491–494, May, 1960. 2 figs., 9 refs.

This paper from Bowman Gray School of Medicine, Winston-Salem, North Carolina, describes the case of a 2-year-old boy who, following operation for excision of a meningomyelocele, developed increased intracranial pressure with papilloedema and bilateral paralysis of the 6th nerve. His resting electroencephalogram (EEG) was made up of diffuse activity at 6 to 7 c.p.s., with some random delta activity. During one recording he had a tonic fit with loss of consciousness. For 5 minutes before the attack the EEG showed high voltage, bilaterally synchronous, rhythmic delta activity, but during the attack there was an absence of electrical activity in all leads. Subsequently the EEG returned to its resting state. The authors consider that the attack was associated with a sudden increase in the cerebrospinal-fluid pressure which gave rise to arteriolar and capillary " shut down ".

A further case is described in which tonic fits occurred without loss of consciousness in an epileptic, who later became mentally defective after a period of unconsciousness lasting 7 months. During these attacks alpha-wave activity disappeared from the record, but fast activity persisted.

[These latter attacks are unlikely to have been true " tonic fits".] *L. G. Kiloh*

1267. **Epilepsy and Neurosis—an Electroencephalographic Problem.** (Épilepsie et névrose—problème EEG)

M. B. Dell and G. C. Lairy. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **12**, 385–398, May, 1960. 8 figs., 20 refs.

In the great majority of cases the electroencephalograms (EEGs) of neurotic patients are easily distinguished from those of epileptic patients, though occasionally the EEGs obtained from neurotic patients do show subclinical paroxysmal discharges. In many neurotic states the symptoms have a paroxysmal quality—for example, in anxiety attacks, obsessional phenomena, impulsive behaviour, and outbursts of anger.

In the study here reported from the Hôpital Henri-Rousselle, Paris, no EEGs recorded in such episodes were available, but records were obtained during hysterical crises and tics, phenomena which can be provoked by suggestion. No paroxysmal discharges were found to accompany tics, and when they did occur in the same patient they appeared independently. In hysterical episodes the EEG is usually reported as being unchanged, but in a number of such cases the authors found that there were some changes, but that these were often in the direction of normality, theta activity disappearing and alpha activity becoming more regular. In patients suffering from both epilepsy and neurosis exacerbations of the neurotic symptoms are sometimes associated with reinforcement of the epileptic discharges. In one case of Jacksonian epilepsy attacks associated with a focal EEG abnormality could be provoked by suggestion.

Of a series of 21 patients with obsessional neurosis without paroxysmal symptoms of any kind, 5 showed epileptic features in the EEG on overbreathing. Similar discharges were seen in 7 out of 75 cases of psychopathy and 8 out of 20 cases of hysteria. It was noted that during interviews with neurotic patients the mention of emotional topics did not give rise to paroxysmal EEG discharges, even though clinical reactions were provoked, but in epileptics such discharges were frequently observed. In those neurotic patients in whom paroxysmal EEG discharges occur, the authors believe that the administration of anticonvulsant drugs may lead to improvement in both the EEG and the symptoms. They also noted that in 3 cases of obsessional neurosis successful treatment with continuous narcosis or deep insulin coma led to a disappearance of paroxysmal abnormalities in the EEG. In other cases similar results were claimed to result from psychotherapy. *L. G. Kiloh*

1268. **Electroencephalographic Studies of Conditional Cerebral Response in Epileptic Subjects**

J. R. Stevens. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **12**, 431–444, May, 1960. 8 figs., 28 refs.

It has been shown that sensory and emotional stimuli may aggravate the tendency to paroxysmal activity in the electroencephalogram (EEG) of epileptic patients. If this response can be regarded as within the range of " adaptive " organismal behaviour, then it might be expected that epileptic paroxysms should be susceptible to conditioning and even to " deconditioning ".

In a study here reported from the University of Oregon Medical School, Portland, 4 epileptic patients with reliable spike–wave responses to photic stimulation were selected for the test. In 2 of these cases a tone signal was paired with photic stimulation, but in the other 2 the tone signal was sounded 2 seconds before the light stimulus. Both tone and light were continued until a spike-and-slow-wave response occurred, and in fact such a response to the light was obtained in 93% of 521 presentations. No evidence of conditioning to the tone was obtained. When procedures likely to be associated with conditional inhibition were used—namely, extinction, differentiation (using another tone signal as a differential stimulus), and retardation—subsequent sounding of the tone unreinforced by light flicker was accompanied by a highly significant increase in spike-and-slow-wave responses. In a second group of subjects 19 epileptics with well developed occipital frequency-specific photic " driving " responses to flicker were investigated, but attempts to condition this phenomenon were unsuccess-

ful, though again there was a significant increase in epileptiform discharges in the EEGs after using extinction and differential stimuli.

Previous workers have reported the occurrence of slow-wave activity in the EEG when conditional inhibition is induced and this, the author suggests, may be an important factor in causing the significant increase of paroxysmal discharges that follows the exposure to conditioned stimuli under these circumstances. She rejects the view that the responses are simply due to drowsiness.

L. G. Kiloh

1269. **Electroencephalographic Study of the Signs of Chronic Vascular Insufficiency of the Sylvian Region in Aged People**

J. H. Bruens, H. Gastaut, and G. Giove. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **12**, 283–295, May, 1960. 4 figs., 49 refs.

From a collection of some 7,000 electroencephalograms taken at random the authors, working in the Netherlands, France, and Italy, have selected 66 which showed the presence of rhythmical, paroxysmal, delta-wave activity in one or both temporal regions. In 70% of these there was a left-sided predominance. The frequency of this pattern increased with age and 50% of the recordings selected had been obtained from patients over the age of 70 years. A study of the clinical records showed that in 61% of the cases "definite" vascular lesions were present and in a further 17% similar lesions were thought to exist. In spite of the rhythmical nature of the discharge the authors consider that it is cortical rather than centrencephalic in origin and that it results from a relative ischaemia of the Sylvian region due to arteriosclerosis of the extra- and intra-cerebral vessels.

In a few additional similar cases observed after this series had been collected, carotid compression on the same side as the delta activity led to an increase in its amount. Inhalation of nitrogen augmented the delta activity, whereas the inhalation of 80% oxygen in some cases led to its disappearance. The authors suggest that it is important to recognize the vascular origin of the pattern described, in order to avoid an unnecessary and erroneous diagnosis of cerebral tumour. They point out that recognition of the pattern is also important prognostically, because it indicates a state of chronic vascular insufficiency, with all that this implies.

L. G. Kiloh

1270. **Effect of Blood Volume and Cardiac Output on the Measurement of Myoclonic Threshold.** [In English] M. V. Driver. *Epilepsia* [*Epilepsia (Amst.)*] **1**, 255–263, April, 1960. 5 figs., 21 refs.

When determining the "myoclonic threshold" the result is usually expressed as the amount of "metrazol" (leptazol) intravenously administered which, when corrected for the patient's weight, produces a defined end-point in the electroencephalogram. The author of this paper from the Institute of Psychiatry, University of London, points out, however, that the quantitative effects of any drug depend upon the concentration at its site of action—in this case the brain. Leptazol concentration cannot be determined in the living brain and can be estimated in the blood only with difficulty. The results are reported of investigations which show a close correlation between the photo-leptazol threshold, blood volume, and cardiac output. The threshold is not significantly related to body weight. These conclusions are based on the assumption that drugs injected intravenously (in this case leptazol) will have similar concentration-time relationships to the indicators used in blood-flow measurements. If the mean arterial concentration of leptazol at the threshold is calculated on this basis a much more homogeneous series of results regarding cerebral excitability is obtained, even when the threshold dosage is expressed in terms of body weight.

J. B. Stanton

BRAIN AND MENINGES

1271. **Reduction of Intracranial Pressure with Hypertonic Urea**

J. Stubbs and J. Pennybacker. *Lancet* [*Lancet*] **1**, 1094–1097, May 21, 1960. 2 figs., 10 refs.

Cerebral oedema is one of the commonest and most urgent problems in neurosurgery and is responsible for many of the symptoms of expanding intracranial lesions, difficulties at operation, postoperative complications, and incomplete recovery. Among measures to reduce this "brain swelling" are elevation of the head, removal of cerebrospinal fluid, and "dehydration" by intravenous infusion of hypertonic solutions of sodium chloride or glucose. More recently anaesthetic techniques such as induced hypothermia or controlled respiration of the curarized patient have been employed.

The authors of this paper from the Radcliffe Infirmary, Oxford, describe the use of intravenous infusion of a solution of urea, which seems superior to and more generally effective than any other substance in reducing intracranial pressure. The method employed was that recommended by Javid in 1958 (*Surg. Clin. N. Amer.*, **38**, 907) and the results obtained in 129 patients over a period of 11 months confirm his findings.

Patients were given 1 to 1·5 g. of urea per kg. body weight as a 30% solution in 10% invert sugar, the optimal rate of administration being 60 drops per minute. The effect was seen within 15 to 20 minutes of starting the infusion and persisted for 4 to 8 hours. In patients undergoing craniotomy the infusion was begun at the same time as induction of anaesthesia, the main effect being a decrease in brain bulk, which made operation easier and safer. The authors state that although arterial oozing was often increased in the early stages of operation, this was more of a nuisance than a danger. The fall in intracranial pressure was measurable by lumbar puncture. No major toxic effects were observed; local reactions were seen in the vein used, but they never progressed to thrombosis. The blood urea level rose and diuresis began shortly after the infusion was started; hence urea should not be given to patients with impaired renal function. The authors suggest in conclusion that apart from its use during brain operations urea may help: (1) to tide over a comatose patient until he can be ad-

mitted to a neurosurgical centre; (2) in treating the post-operative "second-day slump"; (3) in cases of acute head injury or tuberculous meningitis in which the intracranial pressure is high; (4) in relieving benign intracranial hypertension. The most likely mechanism of this reduction of intracranial pressure is by means of a blood–brain barrier to urea. *J. V. Crawford*

1272. **The Osmotherapy of Cranial Hypertension.** (Zur Osmotherapie der intrakraniellen Drucksteigerung)
G. SCHARFETTER, A. HUNZIKER, and A. BÜHLMANN. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **90**, 342–345, March 19, 1960. 3 figs., 8 refs.

After a brief review of the history of methods of lowering the cerebrospinal-fluid (C.S.F.) pressure by means of hypertonic solutions the authors present, from the University Neurological and Medical Clinics, Zürich, a description of the treatment of over 100 patients with urea. This substance was administered by intravenous drip in a solution containing 30% of urea at a rate of approximately 60 drops per minute; the total volume infused was between 200 and 300 ml., this amount being based on an average dosage of 1·0 to 1·5 g. of urea per kg. body weight.

In 10 cases simultaneous recordings of the lumbar C.S.F. pressure, arterial blood pressure, and electrocardiogram were made and these showed that the C.S.F. pressure began to fall and the arterial blood pressure to rise slowly some 20 to 30 minutes after starting the drip. A marked fall in the C.S.F. pressure was obtained in all cases and was maintained for several hours after the infusion was completed; also it was not followed by a rebound above the original level of pressure. The only side-effects of the treatment were headache and occasional vomiting. In 5 patients who were also treated with 25% mannitol intravenously there was a similar but less marked fall in the C.S.F. pressure. The authors discuss the mode of action and indications and contraindications of this " osmotherapy ". *J. B. Stanton*

1273. **Preliminary Observations on Abnormal Catecholamine Metabolism in Basal Ganglia Diseases**
A. BARBEAU. *Neurology* [*Neurology (Minneap.)*] **10**, 446–451, May, 1960. 3 figs., 33 refs.

The suggestion contained in reported studies that a disorder of metabolism of catechol amines may be present in certain conditions affecting the basal ganglia, led the author, at the University of Chicago Clinics, to examine the urine of affected patients for pressor amine substances. The iodine test of Simola for adrenaline-like substances and a bio-assay method for pressor amines detected by the contractions of a strip of rabbit aorta were used. Sjoerdsma's method of qualitative determination of 5-hydroxyindoleacetic acid (5–HIAA) was employed in all cases and chromatography for amino-acids was carried out on a few appropriate samples.

The results with both the bio-assay method and the iodine test were positive in 60% of cases of basal-ganglia disease, in contrast to 2·3% of cases of other disorders. The response to the 5–HIAA qualitative test was negative in all instances. Sometimes the amount of pressor amine substances was as high as that found in cases of phaeochromocytoma; the highest levels were observed in the days following chemopallidectomy in 2 cases in which determinations had proved negative before operation.

Although the chemical nature of the substances detected has not been determined the author considers that these findings strongly indicate that there is a basic metabolic disturbance underlying many basal-ganglia diseases. *J. B. Cavanagh*

1274. **Generalized Reticulosis with Unusual Involvement of the Nervous System.** (Generalisierte Reticulose mit ungewöhnlicher Beteiligung des Nervensystems)
F. FUNK and A. STAMMLER. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete* [*Fortschr. Neurol. Psychiat.*] **28**, 237–247, April, 1960. 5 figs., 26 refs.

A case of reticulosis is described from the University Neurological Clinic, Cologne, in which there was an unusual involvement of the nervous system. The initial clinical picture was that of a para-myeloblastic leukaemia, which remitted after cytostatic therapy. However, during the course of the illness, which lasted 5 years, a polyneuritic syndrome developed which involved the cranial nerves and was accompanied by raised intracranial pressure. Anatomically there was a diffuse reticulosis, with interstitial spread of tumour cells into the internal organs, meninges, nerve roots, peripheral nerves, and around the cerebral vessels.

On the basis of this and other reported cases the authors propose the following classification. (1) Primary reticulosis (primary cerebral sarcoma of the retothelial system). (2) Circumscribed reticulosis starting from the nasopharynx, the paravertebral lymph nodes, and the vertebral column, with defects due to compression of the brain or spinal cord or more rarely to destructive growths in nervous tissue. (3) Cerebral metastases. (4) Generalized reticulosis without any circumscribed tumour formation, that is not a space-occupying tumour but rather one infiltrating the meninges, brain, spinal cord, and peripheral nerves. The case described above belongs to Group 4. *J. Hoenig*

1275. **Relation of Certain Diagnostic Features of Carotid Occlusion to Collateral Circulation**
A. SILVERSTEIN, G. M. LEHRER, and R. MONES. *Neurology* [*Neurology (Minneap.)*] **10**, 409–417, April, 1960. 3 figs., bibliography.

The authors have attempted to correlate the results of certain procedures reported to be diagnostic of carotid artery occlusion with the appearances on angiography of the collateral circulation in 30 patients at Mount Sinai Hospital, New York, with proved occlusion of the common or internal carotid artery. Diminished carotid pulsation was noted in only 5 patients and increased carotid pulsation on the occluded side in 2. Carotid pulsations in the neck or pharynx were found to be of limited diagnostic value, except in occlusion of the common carotid artery, when both the carotid and superficial temporal pulses might be absent. No correlation was found between unequal carotid pulsation and col-

lateral circulation. Carotid or intracranial bruits were of little diagnostic help; with complete occlusion a bruit might be heard on the opposite side, or with partial occlusion, on the same side. Differences in the systolic pressure in the retinal artery greater than 20%, as determined by ophthalmodynamometry, constituted an excellent test for the presence of carotid occlusion; of 20 patients adequately examined 16 had significantly diminished retinal artery pulsations on the side of the occlusion. Manual compression of the patent carotid artery gave valuable information in 21 cases, although there were some false positive results. A correlation was observed between a positive response to the compression test and collateral circulation via the anterior communicating artery. *Hugh Garland*

1276. **Survival after Apoplexy: a 5-Year Follow-up.** [In English]
H. DROLLER. *Gerontologia clinica* [*Geront. clin. (Basel)*] **2**, 120–127, 1960. 10 refs.

The intake of elderly hemiplegic patients into a geriatric unit during 1952 has been reviewed over a period of 5 years. The initial high mortality figure of the immediate effects of the stroke fell to a low level after the first month. A satisfactory proportion of patients could be discharged. However, after 3 years only 32% of the initial 275 patients remained alive, and after 5 years, 22%.—[Author's summary.]

NEUROMUSCULAR DISEASES

1277. **The Place of Corticotropin in the Treatment of Myasthenia Gravis**
L. D. FREYDBERG. *Annals of Internal Medicine* [*Ann. intern. Med.*] **52**, 806–818, April, 1960. 13 refs.

The place of corticotrophin in the treatment of myasthenia gravis is discussed with reference to the results obtained in 5 cases and the personal experience of the author, who has suffered from myasthenia gravis since 1938. The drug was given in a dosage of 100 units daily for 5 consecutive days. It is claimed that 5 of the 6 patients experienced relief, including the author, who was treated on 9 separate occasions with " worthwhile remission every time ". [It is unfortunate that the author does not state whether he himself was taking neostigmine in addition.] *Hugh Garland*

1278. **Motor Unit Territory and Fiber Density in Myopathies**
F. BUCHTHAL, P. ROSENFALCK, and F. ERMINIO. *Neurology* [*Neurology (Minneap.)*] **10**, 398–408, April, 1960. 10 figs., 24 refs.

In an investigation carried out at the Institute of Neurophysiology, University of Copenhagen, the number of muscle fibres per cross-sectional area of motor unit (fibre density) were recorded by multiple leads in patients with different forms of myopathy. In pseudohypertrophic muscular dystrophy both motor unit territory and fibre density were lower than in normal muscle. In the facio-scapula-humeral and the shoulder- and pelvic-girdle types of dystrophy the average motor unit territory and the fibre density were the same as in normal muscle. The motor unit territory was reduced in dystrophia myotonica as in the generalized form of dystrophy, but the fibre density was the same as in normal muscle; the findings were similar in polymyositis. *Hugh Garland*

1279. **The Use of " Durabolin " (19-Norandrostenolone-phenylpropionate) in the Treatment of Progressive Muscular Dystrophy.** (Die Anwendung von Durabolin (19-Nor-Androstenolonphenylpropionat) in der Behandlung der Dystrophia musculorum progressiva)
G. BEKÉNY, F. KRAFT, and S. LÁNG. *Nervenarzt* [*Nervenarzt*] **31**, 118–123, March 20, 1960. 23 refs.

The authors describe the use of " durabolin " (19-*nor*-androstenolonephenylpropionate), a new steroid with an anabolic action and minimal androgenic effect, in the treatment of 24 cases of progressive muscular dystrophy seen at the University Neurological Clinic, Budapest, during 1957 and 1958; 9 of the patients were female and 15 male, the latter group including 4 boys under the age of 14 years. During the course of treatment with durabolin no other form of therapy was given. Muscle biopsy was performed in all cases to confirm the diagnosis and the results were assessed by meticulous examination of the motor nervous system. The drug was given in doses of 25 to 50 mg. in a single intramuscular injection once per week, the treatment lasting 3 to 6 months and being repeated in several cases. In those patients in whom treatment produced no apparent effect after 8 weeks it was discontinued.

The results could be divided into four groups, as follows. (1) Marked improvement lasting for several months after the drug was discontinued. (2) Improvement during the treatment, but with relapse when the drug was withdrawn; even so, these patients felt better for up to 6 months after the course. (3) Some improvement during therapy, but relapse and progression of the illness despite further treatment; some of these patients were worse after treatment than before. (4) No change. There were exactly 6 patients in each of the four groups; all 5 cases of ascending pseudohypertrophy in boys fell into Groups 3 and 4. About half the patients showed considerable improvement in their ability to get about. The authors claim that these results are better than those produced by any other drug tried so far in the treatment of this condition.

Side-effects were minimal, and the very mild degree of virilization in 2 women patients was easily reversed. In 2 other female patients virilization occurred only when the dose was increased to 100 mg. per week. Because of the occurrence of frequent erections, treatment had to be discontinued in 2 of the boys after 2 months. Illustrative case histories from each group are described. The authors recommend a weekly dose of 50 mg. for adults and 20 to 25 mg. for children. The results of various laboratory investigations are presented in a table. The mode of action of the drug is thought to be through nitrogen retention. The authors have also made use of the anabolic effect of durabolin in the treatment of 3 cases of polymyositis. *M. R. Medhurst*

Psychiatry

1280. **Morbidity in a London General Practice: Social and Demographic Data**
L. STEIN. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **14**, 9–15, Jan. [received May], 1960. 2 figs., 4 refs.

The material presented here outlines certain family and social features of the 20% sample of a London group practice, and the consultations made by the adults. In frequency of doctor-consultation and of illness, the patients in the London practice appeared similar to those of other general practices; and in family and social features the patient sample consisted of ordinary families, stable in their homes and jobs, and having social contacts in the area and relatives near-by. The psychiatric hospital rate, both out-patient and in-patient, was relatively low compared with national hospital data. Against this background there was no reason to expect either extremely low or extremely high rates of psychiatric ill-health; yet, as shown elsewhere [Shepherd *et al.*, *Proc. roy. Soc. Med.*, 1959, **52**, 269], high rates were in fact found, and, from the general characteristics of the patient-sample, it would appear unlikely that these were due to abnormal family or economic pressures. In the present study, no association with family characteristics such as size or occupational class, or with family history of mental illness, has been found; perhaps further studies may produce more positive findings.—[Author's summary.]

1281. **Psychiatric Morbidity in a London General Practice**
W. I. N. KESSEL. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **14**, 16–22, Jan. [received May], 1960. 11 refs.

The one-year prevalence rate for persons with conspicuous psychiatric morbidity (C.P.M.) in a London group general practice was 9%. A further 5% had personality defects not associated with their presenting illnesses. In both categories there were more women than men, but the rates were largely independent of age.

Only 3 out of 86 C.P.M. patients had psychoses. Most suffered from anxiety states, and 36 presented psychological symptoms; 10% of the C.P.M. patients were referred to a psychiatrist during the year. Using a modification of the International Statistical Classification of Diseases [World Health Organization (W.H.O.), 1948–9], the author found that C.P.M. patients recorded an excess of mental illness, of illness loosely referable to the nervous system, and of ill-defined conditions, chiefly debility, during the survey year. Consultations for other reasons were similar to those for all other attenders. Most of the psychiatric illnesses persisted into the year following the survey. The C.P.M. patients had much higher mean annual consultation rates than the other attenders, though the average number of their consultations for physical diseases was the same. The high consultation rates of these patients were also present in the years before and after the study year and were not solely due to an excess of very frequent attenders. C.P.M. patients were responsible for 23% of all consultations, but only half of these were for their psychological illnesses. Of all consultations 7% dealt directly with psychological symptoms. C.P.M. patients did not differ from others in respect of measured social factors, but the doctors mentioned domestic and family problems as important determinants in 20% of cases.

The difficulties of delineating and classifying psychological illnesses in general practice are discussed. The extent to which use of the W.H.O. system of classification underestimates such morbidity and the need for strict criteria are stressed.—[From the author's summary.]

1282. **Characteristics of Forty-four Patients Who Subsequently Committed Suicide**
A. D. POKORNY. *A.M.A. Archives of General Psychiatry* [*A.M.A. Arch. gen. Psychiat.*] **2**, 314–323, March, 1960. 1 fig., 9 refs.

The author of this paper from Baylor University College of Medicine, Houston, Texas, studied the characteristics of 44 ex-Service patients, aged 25 to 63 years, who had been treated in hospital and who subsequently committed suicide; all except 5 had received psychiatric treatment. In 22 cases suicide was by gunshot wound. Of the 44 patients, 20 committed suicide within a month of leaving hospital, and 33 had communicated their intention to do so. The author found no indication that the "likelihood of suicide increased disproportionately with age" and no correlation between suicide and religion, marital status, previous military rank, or occupation. Compared with a control group of psychiatric cases the suicide group included more acute cases—that is, more patients in whom the duration of symptoms (mostly depression) was less than one year. Physical illness was of little significance. In patients who committed suicide there was a greater tendency than normal to attacks of rage and often a family history of depression. Alcohol was not an important factor.

In 9 of the 44 patients "suicidal precautions" had been taken, compared with one out of 44 controls. The author discusses the possibility and practicability of predicting suicide and the paradoxical situation in which each prediction is also a decision to prevent the predicted event. *Gavin Thurston*

1283. **Amnesia and Homicide: a Study of 50 Murderers**
B. A. O'CONNELL. *British Journal of Delinquency* [*Brit. J. Deling.*] **10**, 262–276, April, 1960. 19 refs.

From an examination of the records of 50 murderers, originally investigated by Curran, the author found that 20 of them had claimed at one time or another an inability to recollect their criminal act. This, the amnesic group, contained a higher proportion of persons of below

average intelligence (12 out of 20 (60%)), compared with 5 out of 30 (16·5%), and a higher proportion with hysterical personality (10 out of 20, compared with 3 out of 30). Hysterical personality, defined as being characterized by " traits ranging from a persistently immature shallow, egocentric and histrionic mode of behaviour to the capacity to develop and use symptoms for personal advantage ", was the only type of personality to show a special relation to the development of amnesia.

Of the 50 subjects 20 were psychotic, but the incidence of psychosis, mental disorder, criminality, electroencephalographic abnormality, epilepsy, and alcoholism was much the same in both amnesics and non-amnesics. The amnesia was most commonly of the psychogenic type, representing an immediate and easy defence mechanism and the one resorted to most frequently by the more stupid persons. The mental process concerned in the amnesia took the form in most cases of passive disregard rather than active repression of the experience, the memory of the act being simply isolated and ignored. Only 9 of the 50 subjects showed any physiological disturbance in custody; thus 18 (90%) of the 20 amnesics ate and slept well and gained weight in prison compared with 23 (77%) of the 30 non-amnesics, a not very significant difference. The differentiation of organic from psychogenic amnesia is discussed and the difficulty of distinguishing hysterical from malingered amnesia is emphasized, though the legal irrelevance of this is noted, with reference to the recent Podola case. *D. J. West*

1284. **Comparative Study of Attitudes to the Rehabilitation of Psychiatric Patients**
S. FOLKARD. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] 14, 23–27, Jan. [received May], 1960. 5 refs.

A total of 85 patients who had been in a mental hospital [Rehabilitation Unit, Netherne Hospital, Coulsdon, Surrey] for 2 years or more, and had been selected for a programme of rehabilitation, were asked questions about their attitudes to living and working outside hospital. The key-relatives of 57 of these patients were asked similar questions, with a view to identifying shared and differing attitudes, and to assessing the significance which these might have for the subsequent rehabilitation of the patient. Staff views on social prognosis were also obtained, and these were related to the social placement of the patients 2 years later.

Compared with their relatives, significantly more of the patients gave themselves high ratings for their work performance before admission to hospital; thought it had been easy to live with their relatives; thought that their prospects of discharge from the hospital were good; expressed a preference to be discharged rather than to stay in the hospital; were confident of their ability to perform a job of work outside the hospital. Many of the patients seemed capable of living and working in the community, but did not want to leave the hospital, and this attitude appears to be one of the main obstacles to rehabilitation. The patient's self-prognosis and the prognoses given by the staff of the Rehabilitation Unit were shown to be significantly accurate in relation to the social placement of the patients 2 years later. Differences in judgment amongst the staff appear to be related to differences in their optimism and confidence.

The further outcome of the social placement of the patients will be assessed by a follow-up study of those patients who return to live in the community. This will be undertaken one year after they have left the hospital. —[From the author's summary.]

1285. **The Frequency of the Positive Sex-chromatin Pattern in Males with Mental Deficiency**
H. D. MOSIER, L. W. SCOTT, and L. H. COTTER. *Pediatrics* [*Pediatrics*] **25**, 291–297, Feb., 1960. 6 figs., 19 refs.

At the University of California School of Medicine, Los Angeles, examination by the oral smear technique of 1,252 male mentally subnormal patients showed that 10 (0·8%) had a positive sex-chromatin pattern. In these 10 cases the I.Q. ranged from 22 to 66, although of the whole group over 300 had an I.Q. of 19 or less and 37 one of 70 or more. In the 9 postpubertal patients the body proportions were eunuchoid and the testes small with tubular fibrosis. Minimal gynaecomastia was present in 6, urinary 17-ketosteroid excretion was slightly reduced in 5, and the urinary gonadotrophin level was raised in 4 of the 9 patients. Mongoloid features were present in one patient and 2 had mongol siblings. The age of the mothers of 8 of the patients averaged 25·5 years at time of delivery. Distribution of the cases according to race or age showed no significant difference from that in the whole series. All 10 patients were in the undifferentiated, familial, or " other " categories of mental deficiency, and appeared to have a passive–aggressive personality with schizoid tendencies.

The incidence of the syndrome of gynaecomastia, high urinary gonadotrophin content, small testes with tubular fibrosis, and hyalinization with preservation of the Leydig cells (Klinefelter's syndrome) in males has been estimated in the general population at 0·1% in Switzerland, and at 0·03% in England, but in newborn males in England at 2·6%. The male individual with this syndrome is not a genetic or chromosomal female, but a chromosomal intersex. From these findings and those in other similar recent studies it appears that Klinefelter's syndrome with a positive sex-chromatin pattern is likely to be associated with mental subnormality, several workers having shown that about 1% of mentally subnormal males have Klinefelter's syndrome whereas the incidence in the general population is less than 0·2%. *G. de M. Rudolf*

1286. **The Occurrence and Treatment of Hypothyroidism among Alcoholics**
M. GOLDBERG. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **20**, 609–621, April, 1960. 22 refs.

The author, while serving with the U.S. Army Medical Corps in Paris, observed 2 alcoholic myxoedematous patients, both of whom spontaneously reported that hormone replacement therapy not only relieved the hypothyroid symptoms but also enabled them to control the desire for alcohol. This experience and the results of animal experiments which suggested that hypothyroidism

might be aetiologically related to addiction to alcohol, prompted a study of thyroid function in 33 alcoholics.

Hypothyroidism was present in 21 of these patients, the diagnosis being based on a lowered serum protein-bound iodine (P.B.I.) level and an increased duration of the contraction phase of the ankle-jerk, recorded electrically. In some cases the serum P.B.I. level was not below the normal range, but failed to rise 24 hours after injection of 10 units of thyroid-stimulating hormone; this, too, was regarded as evidence of hypothyroidism.

In 29 cases treatment was with L-triiodothyronine, the average daily maintenance dose being 100 μg., and in 4 cases with thyroid extract. The response in 15 was regarded as excellent, an excessive intake of alcohol being controlled consistently over a period of treatment lasting at least 6 months. A further 8 patients showed a "good" response—that is, although they occasionally became intoxicated, their habitual alcohol consumption was reduced and their behaviour no longer involved them in any difficulties. The control of alcoholism appeared to follow hormone therapy more frequently in the hypothyroid than in the euthyroid patient. The author also reports that 39 out of 104 non-alcoholic hypothyroid patients noticed a significant decrease in their alcohol intake after the institution of replacement therapy.

H.-J. B. Galbraith

1287. **Clinical Experience in the Treatment of Alcoholism.** (Klinische Erfahrungen bei der Trinkerbehandlung) H. HETZEL. *Wiener Zeitschrift für Nervenheilkunde und deren Grenzgebiete* [*Wien. Z. Nervenheilk.*] **17**, 196–212, 1960. 30 refs.

In this paper from the Innsbruck University Neuropsychiatric Clinic the author reports a marked increase in the number of alcoholics admitted for treatment. In 1955 26% of the male admissions were alcoholics, and this figure rose to 44% in 1956. Altogether within 2 years 129 patients were treated for delirium tremens. Legislation to secure the admission of chronic alcoholics to clinics and mental hospitals was apparently introduced in Austria in 1957, but with doubtful results.

W. Mayer-Gross

PSYCHOSOMATIC MEDICINE

1288. **Psychotherapy in Migraine**
R. A. HUNTER and I. P. ROSS. *British Medical Journal* [*Brit. med. J.*] **1**, 1084–1088, April 9, 1960.

At the National Hospital for Nervous Diseases, Queen Square, London, a study was made of the part played by emotional factors in the aetiology and persistence of migraine in 35 patients who had shown little or no response to medical treatment. After examination to exclude any physical conditions known to precipitate or aggravate migraine simple psychotherapy was carried out. The 20 female and 15 male patients aged from 21 to 59 were followed up for a period of 6 to 12 months. They were not representative of the migraine population as a whole in that they had particularly severe and frequent headaches which as stated had responded poorly to the usual remedies. The mean duration of the migraine was 11½ years. A family history of migraine was obtained in 18 cases. In general, women patients in the series were more incapacitated than men.

All the patients manifested some degree of psychological disturbance, anxiety and depression being especially frequent, and the migrainous attacks were observed to be closely associated in many instances with stressful interpersonal events, examples of which are given. Treatment by means of psychotherapy led to "significant improvement" of the migraine in 33 cases (94%), lessening of emotional disturbance in 30 (86%), and diminution of drug intake in 34 (97%). A number of the patients, however, remained liable to further attacks of migraine when any untoward events of a distressing nature occurred.

A. Balfour Sclare

1289. **Psychophysiological Influences on Peripheral Venous Tone**
S. I. COHEN, S. BONDURANT, and A. J. SILVERMAN. *Psychosomatic Medicine* [*Psychosom. Med.*] **22**, 106–117, March–April, 1960. 4 figs., 33 refs.

From the U.S. Air Force Base, Dayton, Ohio, is reported a series of observations of psychogenic changes in venomotor tone in 10 healthy volunteers aged 18 to 38. The provocative emotional auditory stimuli consisted of a group of words generally considered to be psychologically arousing. The effect of these "charged" words was compared with that of a group of "bland" words. To detect changes in venous tone an isolated vein segment in the forearm was catheterized and venous pressure recorded continuously. The pulse rate, skin resistance, and electroencephalogram (EEG) were also recorded in order to assess any changes in the level of arousal of the subjects when exposed to the stimuli. In addition to 4 charged and 4 bland words, 4 silent periods were introduced as a control measure.

In response to the charged words the changes in venous pressure were significantly greater than those following the bland words, which in turn produced greater changes than did the silent periods. In all but one of the subjects the increased amplitude of change in the skin resistance after presentation of the charged words was greater than after the bland stimuli. (Changes in pulse rate and EEG are not discussed in this paper.) The authors conclude that the psychologically induced venous changes are probably mediated by autonomic impulses and postulate that such impulses are initiated by a state of arousal in the central nervous system. The findings emphasize that emotional stress may operate via the venous system, as well as through the arterial system or upon the myocardium.

A. Balfour Sclare

1290. **The Family in Psychosomatic Process: a Case Report Illustrating a Method of Psychosomatic Research**
J. L. TITCHENER, J. RISKIN, and R. EMERSON. *Psychosomatic Medicine* [*Psychosom. Med.*] **22**, 127–142, March–April, 1960. 5 figs., 7 refs.

At the Department of Psychiatry of the University of Cincinnati, Ohio, a psychodynamic study was undertaken of an entire family, in which one son (the patient) developed ulcerative colitis. In particular, the network

of relationships within the family was intensively investigated in the manner of the cultural anthropologist. The relevance of the mutually interlocking family relationships to the patient's illness was evaluated. The method of investigation included psychiatric interviews with various members of the family, a " family interaction session ", and an inventory of intra-family relationships. This technique had the advantage of permitting the observers to record a number of varying commentaries upon the same current issues, while in addition useful information was gained during psychotherapeutic sessions with the patient. When first seen by the authors the patient was 24 years old, the third child and second son of the family. It was found that his ulcerative colitis began in relation to his mother's withdrawal and irritability, which was attributed to the menopause, his father's pressure upon him to become more self-reliant and self-supporting, and his own increasing sense of obligation to marry a girl to whom he was half engaged. He had always been overprotected by his mother, while she in her turn had had little affection in marriage. He was also criticized by his brother and sisters.

The matrix of family relationships is depicted schematically. The family is considered as a complex social system in which the most significant psychodynamic issue is not the impact of the mother upon the child, but rather that of the " family's mother " who relates herself to the child in response to multiple influences which in turn impinge upon her. The family studied here was characterized by an " anxious cohesion ", that is, a state of family cohesion achieved at the price of considerable anxiety to each individual concerned.

A. Balfour Sclare

SCHIZOPHRENIA

1291. **Production of Differential Amnesia as a Factor in the Treatment of Schizophrenia**

D. E. CAMERON. *Comprehensive Psychiatry* [*Comprehens. Psychiat.*] **1**, 26–34, Feb. [received May], 1960. 11 refs.

The author describes his " depatterning " treatment of paranoid schizophrenic patients, which consists in the application of electric shocks twice a day, or in sleep treatment for at least 25 to 40 days, or, most effectively, in a combination of these two procedures. This method of treatment has now been extended to other forms of schizophrenia, to intractable alcohol addiction, and to some cases of chronic psychoneurosis.

Three stages of depatterning can be discerned during treatment: (1) extensive loss of recent memory without disorientation; (2) disorientation about which the patient worries; and (3) complete amnesia for anything but the immediate present. After a week in the third stage the treatment is gradually reduced. As the patient returns to earlier stages of depatterning, he may pass through a phase of " turbulence ", with symptoms of anxiety, aggression, and confusion, requiring medication with tranquillizers. As the sphere of total amnesia constricts, differential amnesia occurs, blotting out the memories of past schizophrenic behaviour; this is regarded as a good prognostic sign. The loss of these memories is assisted by a careful avoidance of any questions that might remind the patient of his previous symptoms. If, on return to the first stage, schizophrenic symptoms reappear treatment is again intensified so that the patient returns to the third stage. In rare instances this procedure has to be repeated several times. The symptoms most difficult to eliminate are lack of interest and emotional warmth and inability to relate to others.

This treatment was given in 53 cases of schizophrenia, " a number of cases " of long-term psychoneurosis, and a few cases of addiction seen at the Allen Memorial Institute, McGill University, Montreal. An average of 20 to 30 shock treatments were necessary, but some patients needed considerably more. The average duration of sleep treatment was 15 to 30 days, but in some patients it continued up to 65 days. After the completion of treatment, the patients received one electric shock a month. If there were signs of relapse 4 shock treatments were given within 48 hours, the patient remaining ambulant.

F. K. Taylor

1292. **The Clinical Effect of Phenothiazine Therapy in Schizophrenic End States.** (Über den klinischen Effekt bei der Phenothiazinbehandlung schizophrener Endzustände)

F. G. HACKSTEIN. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete* [*Fortschr. Neurol. Psychiat.*] **28**, 145–161, March, 1960. 23 refs.

The therapeutic effect of physical methods of treatment in psychiatric conditions can be described from two aspects: the " effect proper " (*Eigenwirkung*), and the " clinical effect ". The " effect proper " is the psychoorganic syndrome produced by the treatment itself and consists, in the case of phenothiazine, in the following: (1) shift in autonomic balance with peripheral autonomic signs; (2) toxic effects on the liver, skin, bone marrow and elsewhere; (3) neurological symptoms and signs (amyostasis, dystonia); (4) analgesia; (5) sedation in the wider sense; (6) so-called " paradoxical " irritation (that is, turbulence, insomnia, sleep changes, and similar phenomena; (7) euphoria; and (8) inhibition of drive. The " clinical effect " is brought about either by the drug affecting the physical changes underlying the psychosis, or by the " effect proper " in some way opposing the psychotic symptoms. In the first case one may speak of " radical " therapy, the effects of which are lasting. In the second case the treatment is " symptomatic " and transient. Sometimes, however, the psychotic process changes spontaneously while symptomatic treatment goes on, and after cessation of the treatment a lasting effect appears to have been achieved.

Four types of " clinical effect " can be discerned in schizophrenic patients treated with phenothiazine. (1) The sudden awakening. This occurs mainly in patients with systematized delusions. The entire delusional world is suddenly shaken off and the patient feels as if emerging from a dream. (2) The dissolution of the symptoms. This occurs in cases in which hallucinations dominate the picture. The imagined influences from the outer world lose intensity and become less defined, and

the whole experience of the illness turns into a vague memory. (3) The creation of an adequate attitude to the environment. This occurs in patients who show inadequate, usually hostile, reactions to people. They misinterpret the helpful intentions of others and are unable to appreciate them. These patients often change under treatment, showing a more appropriate response. (4) Reduction of affect. This type of response occurs in patients with a great deal of inner tension, including stupor, and it covers a large number of defect states. Although this reduction appears as an improvement, it does not lead to a disappearance of the schizophrenic experience.

Phenothiazine does not only affect process-schizophrenia, but it also improves end states, and sometimes leads to their remission. Such remissions can only be sustained by maintenance therapy. The remission of the end state is most likely due to a "symptomatic" effect of the treatment. How the therapeutic results are brought about in detail is as yet unknown.

J. Hoenig

TREATMENT

1293. **Thioridazine Therapy: Results and Complications**
R. H. MAY, P. SELYMES, R. D. WEEKLEY, and A. M. POTTS. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **130**, 230–234, March, 1960. 4 figs., 6 refs.

At Cleveland Psychiatric Institute and Hospital, Ohio, thioridazine was tried in the treatment of 29 patients suffering from a variety of psychiatric disorders. It has been reported that this drug has relatively few side-effects and does not cause the extra-pyramidal disturbances usually seen with other phenothiazine drugs. Of the 29 patients, 23 improved. However, in 4 out of 5 patients given more than a total of 85 g. of thioridazine a pigmentary retinopathy developed, the patients complaining of diminution and brownish colouring of vision 20 to 55 days after the start of treatment. Objectively, pigmented deposits were seen in the retina, and in 2 patients there was a loss of night vision and a decrease in central visual acuity. It is suggested that the maintenance dose should never exceed 800 mg. a day, and that the drug should be discontinued if any ocular symptoms or signs appear. Other side-effects were not a problem, and mild extra-pyramidal disturbances occurred in only a few patients receiving large doses of the drug.

B. M. Davies

1294. **A Pilot Trial of Orphenadrine ("Disipal") in Patients Treated with Reserpine**
G. E. LANGLEY and A. A. ROBIN. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 682–685, April [received June], 1960. 14 refs.

Used in doses of 50 mg. t.d.s. no evidence is forthcoming from this small series of patients that the combination of orphenadrine with reserpine (0·5 to 2 mg. t.d.s.) is of clinical value in mitigating the less severe extra-pyramidal and other side-effects of reserpine. Likewise, no evidence was found for a sedative action or for a significant enhancement of the tranquillizing properties of reserpine as measured by a motor test and behaviour rating scale respectively. The value of orphenadrine in severe states of reserpine intoxication has not been tested. Nevertheless, the dosage of reserpine used in this trial is frequently employed in psychiatric practice and in the light of the above evidence it would appear unjustified to combine orphenadrine with it in a routine fashion. Such a combination, moreover, increases the cost of reserpine medication approximately tenfold.—[Authors' summary.]

1295. **Deanol in Depression: a Controlled Trial**
J. DOMINIAN. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 711–712, April [received June], 1960. 3 refs.

Deanol, a drug reported to be useful in mild depression, was studied in a controlled trial using 20 patients. The results obtained were no better than those of the placebo. —[Author's summary.]

1296. **Some Observations on Psilocybin, a New Hallucinogen, in Volunteer Subjects**
S. MALITZ, H. ESECOVER, B. WILKENS, and P. H. HOCH. *Comprehensive Psychiatry* [*Comprehens. Psychiat.*] **1**, 8–17, Feb. [received May], 1960. 1 fig., 18 refs.

The mushroom *Psilocybe mexicana* Heim is used by remote Indian tribes in Southern Mexico to produce hallucinatory phenomena during religious rituals. The active psychotropic principle, "psilocybin", which was isolated from the mushroom, is a hydroxytryptamine derivative, closely related to serotonin.

The authors of this paper from New York State Psychiatric Institute studied the effect of psilocybin in 14 student volunteers (12 male and 2 female, aged 20 to 27 years) who had never shown any neurotic or psychotic symptoms. The drug was administered in a semi-darkened room and the dose ranged from 8 to 36 mg. The responses to the drug were similar to those seen after administration of LSD-25 (lysergic acid diethylamide). Most subjects reported visual hallucinations, especially of coloured forms, but also of more elaborate scenes. Visual illusions were common, auditory illusions less so. Among other mental symptoms were body-image disturbances, alterations of mood (euphoria, anxiety, depression), disorganized thinking, distractability, flight of ideas, pressure of speech, paranoid and grandiose tendencies, and concrete interpretations of proverbs. Pupillary dilatation was present in all subjects. Some complained of nausea, dizziness, flushing, and abdominal discomforts. In 3 there were changes in blood pressure and pulse rate. Paraesthesiae and yawning were also noted. Drug effects in the Indian tribes had included signs of religious ecstasy, but these were absent among the subjects of the present trial, no doubt because of the difference in setting and in expectations.

The effect of the drug was first noticed 30 to 60 minutes after ingestion and reached its height after 1½ to 2½ hours. Among after-effects, headaches and drowsiness were common. The authors warn against the use of hallucinogenic drugs in the treatment of out-patients because of the danger of acute excitement or depression with suicidal tendencies.

F. K. Taylor

Paediatrics

NEONATAL DISORDERS AND PREMATURITY

1297. **Nasal Staphylococci and Sepsis in Newborn Babies**
P. A. MANFIELD, R. A. SHOOTER, and O. M. LIDWELL. *British Medical Journal* [*Brit. med. J.*] **1**, 1098–1099, April 9, 1960. 3 refs.

The study herein reported continues a previous investigation (*Brit. med. J.*, 1958, **1**, 74; *Abstr. Wld Med.*, 1958, **24**, 147) carried out at the same unit (St. Bartholomew's Hospital, London) into the problem of the colonization by staphylococci of the noses of newborn infants. Throughout the investigation triple dye was applied at birth and thereafter daily to the umbilical stumps of 312 infants.

Of 110 infants receiving this treatment only 38 (35%) were not carriers of *Staphylococcus aureus* by the 12th day. A group of 97 infants were treated in addition in a nursery in which the air was disinfected by ultraviolet light; this appeared to have no appreciable effect on the colonization rate, swabs from only 35 (36%) of the 97 being still negative for *Staph. aureus* on the 12th day. Finally, 105 infants received in addition to triple-dye treatment daily baths with hexachlorophane; nasal swabs from 48 (46%) of these 105 infants were still negative on the 12th day. There were 24 instances of proven or presumed staphylococcal sepsis in the series. Of these, 20 occurred in the 191 infants who were nasal carriers of staphylococci by the 12th day, an infection rate of 10·5%; the remaining 4 occurred in the 121 children who were negative for the organisms, a rate of only 3·3%. There thus appears to be a definite relationship between nasal colonization and clinical staphylococcal infection in the newborn. *Winston Turner*

1298. **A New Form of Respiratory Disease in Premature Infants**
M. G. WILSON and V. G. MIKITY. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **99**, 489–499, April, 1960. 11 figs., 7 refs.

From Los Angeles County Hospital (University of California) details are given of 5 cases, and reference made to 2 further similar cases, of a serious pulmonary disease with unusual characteristics, in 2 cases resembling the Hamman–Rich syndrome, all occurring in premature infants under 4 weeks old. The onset, manifested by hyperpnoea and cyanosis, was insidious, and there were wheezing, coughing, and over-expansion of the chest without rales and without fever. Cor pulmonale developed with cardiac failure. Electrocardiography revealed progressive right ventricular hypertrophy and the chest radiograph showed coarse infiltration, with small areas of emphysema. Histological examination of the lung in 3 cases confirmed that there was emphysema with interstitial fibrosis and an interstitial mononuclear cellular infiltration. Three of the patients, one Japanese and 2 negro babies, died 62, 232, and 27 days respectively after the onset. The other 2 white babies survived, one with a tendency to recurrent heart failure. No specific bacteria or virus could be identified, nor was there evidence of any associated or underlying defect.
A. White Franklin

1299. **Congenital Biliary Atresia. I. Analysis of Thirty Cases with Particular Reference to Diagnosis**
L. J. KROVETZ. *Surgery* [*Surgery*] **47**, 453–467, March, 1960. 8 figs., 43 refs.

This paper from the University of Minnesota, Minneapolis, presents an analysis of 30 cases of congenital biliary atresia in most of which jaundice was present at birth or appeared within a few days. The main emphasis is on the preoperative differential diagnosis from cases due to non-atretic causes, a feat which the author admits presents great difficulty and necessitates astute clinical observation and accurate laboratory tests. The series consisted of 28 cases of extrahepatic and 2 of intrahepatic atresia. In only 2 of the former was an extrahepatic atresia amenable to operation; one of these infants died of peritonitis and in the other the presence of a duct suitable for anastomosis was overlooked at operation. Full details of the cases and the results are tabulated.

A comparison is made with 24 cases of prolonged jaundice from other causes, namely cirrhosis (4 cases), neonatal hepatitis (9), the so-called inspissated bile syndrome (5), the inspissated bile syndrome following erythroblastosis foetalis (5), and undetermined (1). In this group, by delaying operation or blood transfusion, jaundice, erythroblastosis foetalis, and sepsis can be eliminated since in the majority of these cases the jaundice disappears spontaneously in 4 to 6 weeks. However, in rare cases atresia may be an associated condition. The time of onset of the jaundice is of little help, but generally if dark faeces is passed at any time by an infant with previously acholic stools, atresia is an improbable cause of the jaundice. It was found impossible to distinguish clinically between the inspissated bile syndrome and atresia, and even at operation the distinction may be difficult.

The most valuable laboratory aid was found to be weekly determination of the serum bilirubin level. In cases of atresia there is usually a steady rise to a point of stabilization, although there may be slight fluctuations. In other cases, including the inspissated bile syndrome, fluctuations are wide, but the tendency is for the serum bilirubin level to fall and ultimately to reach normal. Estimation of faecal urobilinogen excretion was of value only in that high normal values excluded the diagnosis of atresia. The results of the thymol turbidity and cephalin flocculation tests and estimation of serum total cholesterol values were not significantly different in the

patients with atresia, but high serum alkaline-phosphatase levels, that is, more than 20 Bodansky units or more than 90 King–Armstrong units, were found only in the atretic cases.

Finally attention is drawn to one case in which instead of bile ducts only fibrous cords were found at laparotomy; the prognosis seemed hopeless, yet this patient is still alive and in relatively good health at 16 years of age with a normal cholecystogram. Thus when a diagnosis of atresia is made, although a very grave prognosis must be given, survival may be prolonged even without successful surgical intervention. *Andrew M. Desmond*

1300. **Congenital Biliary Atresia. II. Analysis of the Therapeutic Problem**

L. J. KROVETZ. *Surgery* [*Surgery*] **47**, 468–489, March, 1960. Bibliography.

One hundred and thirty-seven reported cases of patients with congenital biliary atresia born after Jan. 1, 1945, are reviewed. Of these, 15 were of the intrahepatic variety and 76 lacked extrahepatic ducts of a nature amenable to curative surgery. A critical review of reported series and our own cases reveals that only 19% of these cases offer ducts theoretically suitable for operation. The number of cases actually cured by operation is discouragingly small, a total of only 65 cures having been reported to date. Analysis of the reported series, after eliminating cases that probably did not have congenital biliary atresia, results in a cure rate of 8%.

As mentioned in the first part of this report [see Abstract 1299], at least 14 cases that were thought to be inoperable and given a hopeless prognosis, but who subsequently cleared their jaundice, have now been reported. Among the surgical cures reported, details as to the site of atresia and the presence of dilatation above the atretic site were frequently not reported. I believe that several of these so-called cures might also have had a spontaneous relief of jaundice or might actually have been cases of neonatal hepatitis.

Theoretically, the operation of choice would be the one which most nearly duplicates the normal anatomic biliary flow. However, from the data reported, there does not seem to be any obvious operation of choice in terms of operative success. I was unable to find a single surgical success following hepatoenterostomy, external or internal drainage of bile. Since operative diagnosis is not infallible, the procedure of choice if no correctable atresia can be found, would seem to be not to attempt these procedures at initial exploration. Spontaneous remission of the jaundice or growth of a small duct that did not appear suitable for anastomosis at the time of initial exploration have occurred at later dates and offer more hope than these singularly unsuccessful operations. Unfortunately, no estimate of the time needed for these phenomena to occur can be made from the available literature.

A variety of opinion exists as to the optimal timing of surgical intervention, ranging from less than 4 weeks to more than 4 months. While there is generally a progression of fibrotic changes with age, cases have been reported with severe fibrosis at early ages and other cases with little or no fibrosis at later ages. Analysis of 40 cases in which curative procedures were done and the ages at operation were stated shows relatively little prognostic implication with age until after 4 months of age. Some degree of caution is needed before drawing firm conclusions from these data because of the small numbers involved in the individual age categories. From analysis of the data available pertaining to diagnosis and operative success, conservative watchful management for at least 4 weeks or until the patient is approximately 3 months of age would seem to be the best policy at present.—[Author's summary.]

1301. **Hyperbilirubinaemia in Premature Infants and the Effect of Synthetic Vitamin K**

B. CORNER, E. BERRY, and A. V. NEALE. *Lancet* [*Lancet*] **1**, 715–717, April 2, 1960. 3 figs., 14 refs.

Hyperbilirubinaemia and kernicterus may sometimes occur in premature infants who show no evidence of isoimmunization. In 1955 and 1956 several reports appeared which suggested that the dosage of the synthetic vitamin-K analogue known as "synkavit" or "kappadione" (tetrasodium 2-methylnaphthalene-1:4-diol phosphate) showed a close correlation with the serum bilirubin level. The authors, working at the University of Bristol, have therefore investigated the effect of varying doses of a different vitamin-K analogue, menaphthone dipotassium disulphate ("vikastab"), on the serum bilirubin levels of premature babies admitted to two Bristol maternity hospitals. No infants were included who showed evidence of blood group incompatibility. The serum bilirubin level was estimated on venous blood by a modification of the method of Evelyn and Malloy.

Of the 436 babies studied 107 received no vitamin K, 94 received 5 mg., 138 received 10 to 15 mg., and 97 a total of 30 to 60 mg. of vikastab, all the injections being given in the first 2 days of life. The maximum serum bilirubin level and also that on the 4th day were highest in the most immature babies. When the infants were grouped according to degree of estimated maturity, however, there was no significant difference between the results in the babies who received no vitamin-K analogue and those in the infants who received the varying doses of the vitamin. The authors conclude that in this series the hyperbilirubinaemia was related to degree of immaturity and was unaffected by menaphthone dipotassium disulphate (vikastab) even in relatively high doses.

F. P. Hudson

1302. **ABO Mother–Infant Incompatibilities**

P. O. HUBINONT, A. BRICOULT, and P. GHYSDAEL. *American Journal of Obstetrics and Gynecology* [*Amer. J. Obstet. Gynec.*] **79**, 593–600, March, 1960. Bibliography.

When haemolytic disease of the newborn is due to ABO incompatibility the result of the antiglobulin (Coombs) test is often doubtful or negative. The authors, writing from the University of Brussels, describe a modification of the test which they claim to be of diagnostic and prognostic value under these conditions.

Packed cord erythrocytes are washed, haemolysed, and centrifuged, the stroma being again washed and then incubated with bovine albumin. The resulting suspension is centrifuged and the supernatant tested by the indirect antiglobulin test against A_1, A_2, B, and O erythrocytes. *F. P. Hudson*

1303. **Patterns of Fat Excretion in Feces of Premature Infants Fed Various Preparations of Milk**
M. DAVIDSON and C. H. BAUER. *Pediatrics* [*Pediatrics*] **25**, 375–384, March, 1960. 5 figs., 23 refs.

In a study undertaken at New York Hospital–Cornell Medical Center, New York, to determine whether the steatorrhoea of premature infants is also accompanied by the excretion of large amounts of saturated fatty acids in the faeces, the 57 premature infants investigated were divided into 4 groups and received respectively: (1) a milk mixture low in animal fat, (2) evaporated milk and dextri-maltose, (3) a vegetable-fat formula, and (4) evaporated milk with dextri-maltose and added protein. These diets were given for 4 days and the stools collected during the 48 hours of the last 2 days. The tabulated results show in detail the total fat absorption in the various groups.

On the basis of the findings the authors suggest that, as with other children, steatorrhoea in premature infants need not necessarily be accompanied by diarrhoea. The study also showed that the proportion of saturated fatty acid excreted by the premature infant is directly related to the kind of fat in his diet and not to the proportion of fat which he absorbs with different diets. It is concluded that the source of fat in the stool of the premature infant is virtually all exogenous in origin, and that the wide variations in fat output in the stools normally encountered cannot be accounted for on the basis of endogenous losses. *J. M. Smellie*

CLINICAL PAEDIATRICS

1304. **Allergenicity of Cow's Milk Proteins. I. Effects of Heat Treatment on the Allergenicity of Protein Fractions of Milk as Studied by the Dual-ingestion Passive Transfer Test**
L. V. CRAWFORD. *Pediatrics* [*Pediatrics*] **25**, 432–436, March, 1960. 9 refs.

Infants sensitive to cow's milk have always constituted a problem. Recently, the pure protein fractions of cow's milk have been isolated, and animal experiments have shown that heat denaturation affects the allergenicity of two of the fractions. In this paper from the University of Tennessee and the Frank T. Tobey Memorial Children's Hospital, Memphis, the author describes an experiment designed to demonstrate that infants sensitive to cow's milk can tolerate heat-denatured milk.

The dual-ingestion passive transfer test was used (Ratner *et al.*, *Ann. Allergy*, 1952, **10**, 675). Skin-sensitizing antiserum was obtained to casein, lactoglobulin, and lactalbumin. The volar surface of the forearm of 20 children (aged 3 to 6 years) was injected with antiserum of each fraction in turn; this provided a passive sensitization. After a 24-hour fast heat-denatured milk was ingested. The reaction of the injection sites was noted and when it had subsided (after 3 hours) pasteurized skimmed milk was consumed. The three different fractions were injected at monthly intervals at two sites on each forearm. The results obtained with liquid and powdered heat-denatured milk as against pasteurized skimmed and pasteurized homogenized milk are given in two tables. There were no reactions to the *alpha*-lactalbumin or *beta*-lactoglobulin fractions in heat-denatured milk. These two fractions are responsible for 72% of the cases of sensitivity to milk seen in infants. However, both types of milk produced urticarial reactions at the casein-sensitized sites. The author discusses the possible reasons for the reduced allergenicity of heat-sensitized milk. *M. R. Medhurst*

1305. **Changes in Gamma Globulin in Childhood. II. Hypogammaglobulinaemia and Infantile Eczema.** (Změny gamaglobulínu v dětském věku. II. Hypogamaglobulinémie u kojeneckého ekzému)
J. MASOPUST and G. VOLNÁ. *Československá pediatrie* [*Čsl. Pediat.*] **15**, 289–295, April, 1960. 1 fig., 18 refs.

The changes which take place in the blood proteins in cases of infantile eczema are not uniform and are often contradictory. At the Second University Paediatric Clinic, Prague, the authors examined 41 children aged from 2 to 24 months whom they divided into two age groups, 2 to 5 months and 5 to 24 months. These children were suffering from eczema of differing severity, varying from minute patches on the face to a generalized eczema. In most cases there was no exudation. Separation of the patients' serum protein fractions by paper electrophoresis showed a very slight fall in the total serum protein level in the younger children, but none in the older age group. Significant changes, however, were found in gamma-globulin level, which was below normal in both groups. Administration of gamma-globulin in fractionated doses to 6 of the children resulted in a rise in the serum gamma globulin level with substantial improvement in the eczema.

[In view of the very small number of cases treated no general conclusion can be drawn regarding the value of such therapy in eczema.] *M. Hrusak*

1306. **Psychopathological Studies of Children and Adolescents with Endocrine Disorders. I. Ovarian Dysgenesis and the Adrenogenital Syndrome.** (Psychopathologische Studien bei endokrin gestörten Kindern und Jugendlichen. I. Mitteilung. Ovarialdysgenesie und adrenogenitales Syndrom)
H. WALLIS. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **83**, 420–453, 1960. 1 fig., bibliography.

This is the first of a series of communications from the Hamburg University Paediatric Clinic dealing with the psychiatric changes observed in children showing endocrine disturbances. The author describes the findings of other workers in the field, who are generally agreed that children who have an endocrine imbalance also show abnormal psychological features. The report is divided into two parts, the first dealing with 12 children with a

clear-cut Turner's syndrome, and the second with 6 cases of the adrenogenital syndrome.

The 12 children suffering from Turner's syndrome were all genetically male, but showed the classical stigmata of the syndrome. None of the parents complained of psychiatric disturbance in the children. On questioning they described the children as " girlish ", good-tempered, easy mixers, and very manageable. Their school performance was adequate, and their I.Q. was in the dull normal range. In the Behn–Rorschach test F% ranged from 50 to 100 and V% from 38 to 77; only one original answer was obtained. No mood swings were observed and the children were relaxed and generally passive. They were infantile, lacked originality and initiative, and were very dependent on their families. A series of projection tests showed that all the children assumed female roles. The thing that upset the children most was their physical underdevelopment. Other authors have described psychological maturation after hormone therapy, but the present author is not prepared to comment on her results as yet.

In the second half of the article the author summarizes present-day knowledge on the subject of the adrenogenital syndrome and agrees that gross psychological or intellectual disturbance is uncommon. Six cases in females are described in detail. They give an impression of undeveloped features with bad-tempered, immature emotional reactions. So long as their environment permits they passively accept their large size and male sex. One patient treated early was active, independent, secure, and differentiated. These features of personality get lost as the disease progresses. Any apparent psychopathology is therefore due to the disease and not to neurotic mechanisms. *M. R. Medhurst*

1307. **Anaphylactoid Purpura in Children (Schönlein–Henoch Syndrome): Review with a Follow-up of the Renal Complications**

D. M. Allen, L. K. Diamond, and D. A. Howell. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **99**, 833–854, June, 1960. 6 figs., bibliography.

1308. **Clinical and Hematological Manifestations of Hemoglobin CS Disease in Children**

A. H. Tuttle and B. Koch. *Journal of Pediatrics* [*J. Pediat.*] **56**, 331–342, March, 1960. 2 figs., 42 refs.

The clinical and haematological features in 18 negro children (aged 9 months to 15½ years) with haemoglobin CS disease have been studied at the University of Tennessee, Memphis. The abnormal haemoglobins and their proportions were identified in all cases by paper electrophoresis. In addition to observation of the 18 patients, most of them for several years, the immediate families of 13 were studied with particular reference to the relative proportions of haemoglobins A, C, and S. Painful abdominal and musculo-skeletal " crises " were found to be less frequent and less severe than in haemoglobin SS disease (sickle-cell anaemia). These crises were often preceded by mild infections, and in 4 cases the lowest haemoglobin levels were encountered during the crises. The authors are uncertain whether the crises are haemolytic or are regenerative in type, but both types have been described in haemoglobin CS disease. In most of the patients there was significant enlargement of the liver and spleen, and transient splenomegaly was sometimes associated with crises. In contrast to haemoglobin SS disease, the splenomegaly of haemoglobin CS disease is both progressive and persists into adult life and radiological evidence of bone changes is relatively infrequent, although 2 patients had bilateral aseptic necrosis of the femoral head. The susceptibility to bacterial osteomyelitis of patients with haemoglobin CS disease is discussed, and one such case is described in which the infection was considered to be due to an organism of the *Salmonella* group. Most of the patients were of normal height and weight, but 4 are described as asthenic. There were recurrent respiratory infections in 9 of the children, and these were often followed by crises; such a sequence accounted for the only observed death in this group.

The anaemia of haemoglobin CS disease tends to be less severe than that of haemoglobin SS disease. Sickling was readily induced in haemoglobin CS erythrocytes but target cells in stained smears were very much more common than in haemoglobin SS disease. The osmotic fragility of erythrocytes was not found to be reduced; and reticulocytosis and mild jaundice were inconstant but related to the occurrence of crises. In most cases haemoglobin C predominated over haemoglobin S and most of the patients showed persistence of haemoglobin F. It is suggested that consideration of the clinical and haematological features of the two conditions will usually allow haemoglobin CS disease and haemoglobin SS disease to be distinguished in individual cases [Denny *et al.*, *A.M.A. Arch. intern. Med.*, 1957, **99**, 214; *Abstr. Wld Med.*, 1957, **22**, 34]. *A. G. Baikie*

1309. **Viruses, Bacteria, and Respiratory Disease in Children**

P. S. Gardner, J. P. Stanfield, A. E. Wright, S. D. M. Court, and C. A. Green. *British Medical Journal* [*Brit. med. J.*] **1**, 1077–1081, April 9, 1960. 19 refs.

All children with acute respiratory infection (195) admitted to the Royal Victoria Infirmary, the Babies' Hospital, and the General Hospital, Newcastle upon Tyne, between January 1 and June 30, 1959, have been studied in a further attempt to correlate the clinical, bacteriological, and virological findings. The 146 cases available for the full study and with adequate follow-up were divided into five clinical groups: (1) 28 with upper respiratory infections, (2) 6 with croup, (3) 37 with acute bronchitis, (4) 27 with acute bronchiolitis, and (5) 48 with broncho- or segmental pneumonia. Infection was established by the finding of a positive throat swab or a titre of complement-fixing antibodies rising at least fourfold between initial and convalescent samples of serum.

Virus infection was diagnosed in 35 cases, including 11 of upper respiratory tract infection, 5 of bronchitis, 13 of pneumonia, and all 6 cases of croup, but in no case of acute bronchiolitis; possible reasons for failure to detect virus in this last group are discussed. Each clinical group produced an assortment of viruses with

no predominance of any one type and no association with particular physical signs. The croup-associated virus of Chanock and Beale was incriminated for the first time in Britain in 5 acute cases varying from mild upper to severe lower respiratory-tract illness. There was no correlation between any bacterium and any clinical group. *A. White Franklin*

1310. **Roentgenologic Studies of Respiration in Infants.** [Monograph, in English]
J. F. Bosma, J. Fawcitt, J. Lind, Y. Takagi, and C. Wegelius. *Acta paediatrica* [*Acta paediat.* (*Uppsala*)] **49**, Suppl. 123, 1–69, March, 1960. 40 figs., bibliography.

1311. **Association between Maternal Disease during Pregnancy and Myopia in the Child**
P. A. Gardiner and G. James. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **44**, 172–178, March, 1960. 14 refs.

Some workers have noted an association between congenital myopia and prematurity. The authors have studied two series of consecutive cases of congenital myopia (more than −4 D) from the point of view of maternal disease during pregnancy, and compared the findings with those in a control group of mothers and children suffering from visual disorders other than myopia. Toxaemia (hypertension, pre-eclampsia, or renal disease) occurred in 50% of the mothers of the myopic children, and a further 25% had other well-defined disease. Only 13% of the mothers in the control group had had toxaemia and a further 12% other diseases, usually of a trivial nature. Prematurity was not a feature of the myopic group. It is considered that congenital myopia may be analogous to acquired myopia, since there is evidence that it occurs in a child whose general growth is normal but whose nutrition is abnormal. *E. S. Perkins*

1312. **A Critical Evaluation of Therapy of Febrile Seizures**
J. G. Millichap, L. M. Aledort, and J. A. Madsen. *Journal of Pediatrics* [*J. Pediat.*] **56**, 364–368, March, 1960. 13 refs.

In a controlled trial of the prophylactic treatment of febrile convulsions, children admitted to the Bronx Municipal Hospital Center, New York, during a 2-year period were given phenobarbitone either regularly every day (mean daily dose 3·1 mg. per kg. body weight) or only at the time of each febrile episode (mean daily dose 3·8 mg. per kg.). A small group of 7 children were given diphenylhydantoin regularly (10 mg. per kg. daily). The children receiving continuous medication were given additional phenobarbitone at the time of each feverish illness.

Results in all groups were disappointing; 10 of the 19 receiving intermittent phenobarbitone treatment, 9 of the 21 given continuous treatment, and all 7 receiving continuous diphenylhydantoin treatment had convulsions during febrile illnesses. The tendency to recurrent seizures was greater in those who had 4 or more seizures before inclusion in the trial. Experimental evidence is cited which indicates that in animals much higher and toxic doses of anticonvulsants are needed for the prevention of artificially-induced febrile convulsions than are required for the control of non-febrile seizures. In this series, treatment of patients in the maximum tolerated range of dosage was no more effective than intermittent therapy in average doses. It is concluded that continued administration of anticonvulsants is unwarranted in the prophylactic treatment of febrile convulsions.

[A valuable contribution.] *John Lorber*

1313. **Abdominal Epilepsy**
B. N. Sheeby, S. C. Little, and J. J. Stone. *Journal of Pediatrics* [*J. Pediat.*] **56**, 355–363, March, 1960. 3 figs., 32 refs.

The authors of this paper from the Medical College of Alabama, Birmingham, Alabama, accept the concept of " abdominal epilepsy " and consider that it occurs much more frequently than it is diagnosed. The syndrome is observed predominantly in children and its manifestations are paroxysmal abdominal pain and vomiting. Headaches, syncopal episodes, and somnolence often accompany the abdominal symptoms. The electroencephalogram (EEG) is usually abnormal and often shows the 14 and 6-per-second dysrhythmia described by Gibbs [*Neurology* (*Minneap.*), 1951, **1**, 136]. A series of 19 patients aged 16 months to 35 years (average 11 years) are described and the various features of their symptoms analysed [in percentages]. Just over half the EEG tracings were considered to be abnormal. Treatment with diphenylhydantoin was found to be entirely satisfactory [but the follow-up period was as short as one month in several cases]. Only 2 patients were not improved.

[This paper is no more convincing than many others on the same subject that there is such a condition as " abdominal epilepsy ".] *John Lorber*

1314. **Malignant Tumors in Childhood**
W. B. Kiesewetter and E. J. Mason. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 1117–1121, March 12, 1960. 1 fig.

Malignant disease was diagnosed in 404 of 38,967 children admitted to a hospital [Children's Hospital, Pittsburgh] during 6½ years. In children less than one year old, renal and adrenosympathetic tumors were the most frequent type. Thereafter leukemia and lymphoma predominated until the age of 8 years. In the 10-to-13-year age groups, inclusive, tumors of the central nervous system and eye predominated. Twelve cases of bone tumor were observed, all in children past their second birthday. About one-third of the 404 patients came to medical attention because of a mass. The most frequent error at the initial examination was a diagnosis of upper respiratory infection. The two types of malignancy most frequently misdiagnosed were Hodgkin's disease and neuroblastoma. The fact that 75% of those who died from malignant disease were dead at the end of the first 12 months indicates the need for prompt action when the diagnosis is made.—[Editorial summary.]

Medical Genetics

1315. **Genetics of Convulsive Disorders. I. Introduction, Problems, Methods, and Base Lines**
J. D. METRAKOS and K. METRAKOS. *Neurology* [*Neurology (Minneap.)*] **10**, 228–240, March, 1960. 1 fig., 20 refs.

This paper from McGill University, Montreal, presents a report of the first of a series of studies designed to assess the hereditary factors in the aetiology of the " various epilepsies ". The definition of convulsive disorder, the methods applicable to the whole series, and some original observations on the history of convulsions in a group of children admitted to hospital, and in their relatives, are considered. The main sample consisted of 1,000 patients admitted to the Montreal Children's Hospital; most of these were consecutive admissions in the period January to March, 1956, but a few (27) were included from an earlier study in 1955 as replacements for those in the consecutive series for whom the records were incomplete. An affected child is defined as one who had at least one convulsion irrespective of the cause, while a convulsion is defined as " a series of involuntary contractions of any of the voluntary muscles produced by abnormal neuronal discharges originating within the brain ". Further elaboration clarifies the cases excluded from this definition. Questioning of the mothers revealed that 115 patients were affected and that of these, 30 had been admitted because of their convulsions, while a further 23 had convulsions associated with the condition for which they were admitted. [Rates based on these figures in terms of admissions are quoted throughout, although the 1,000 admissions related to only 941 children. However, the same analyses repeated on the basis of 941 cases did not reveal any significant differences.]

The family histories of 68 of the affected children were compared with those of 132 unaffected children. The sample of 68 was selected at random, but the authors point out that only 97 of the sample of unaffected children were so selected, the remainder being included because family histories were available. They state that they were unable to find any obvious differences between the two sub-samples of 97 and 35 unaffected children and consequently they considered them as one complete sample. [It is doubtful whether this is really valid, since the 35 available family histories had been obtained " originally by some member of the Department of Medical Genetics for reasons other than this particular study ", and this implies some deliberate selection in that they were of some particular interest as a group.] The relatives of affected children were found to include a higher proportion of affected persons than did the relatives of unaffected children. This was true of most degrees of relationship studied and the differences in proportions affected tended to become less as the degree of relationship considered became more distant. If all the near relatives, that is, parents, sibs, aunts, uncles, grandparents, and cousins, were taken into account, then 3·79% of the relatives of affected children were affected, compared with 1·31% of the relatives of the unaffected children.

The authors draw attention to some of the difficulties in interpreting such data, but they conclude that the data do strongly suggest a familial distribution of convulsions among the near relatives of children who have had at least one convulsion. [The authors do not make clear in this paper whether any allowance has been made for the different ages of the groups of propositi and relatives compared, but it is possible that the period of exposure will be considered in a later paper, since studies of more specific diagnostic groups are promised.]

E. A. Cheeseman

1316. **Hereditary Nephritis**
J. A. CHAPPELL and W. M. KELSEY. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **99**, 401–407, April, 1960. 2 figs., 9 refs.

A review of the literature shows that the syndrome of nephritis and congenital deafness has been reported only in 10 families. In this paper from the Bowman Gray School of Medicine and the North Carolina Baptist Hospital, Winston-Salem, North Carolina, 2 further families are described in which several members had both nephritis and congenital deafness. It was possible to study affected members of two generations in each of these families. The pattern of inheritance in these and the other reported families is that of a mutant gene manifesting itself in heterozygotes. Males with the disease usually die from renal failure before the age of 20. Females, on the other hand, are usually less severely affected, renal disease being diagnosed early only by the repeated findings of haematuria; few affected females die before the age of 30. The clinical picture is that of glomerulonephritis, but at necropsy the findings are those of pyelonephritis.

C. O. Carter

1317. **The Enzymatic Expression of Heterozygosity in Families of Children with Galactosemia**
G. N. DONNELL, W. R. BERGREN, R. K. BRETTHAUER, and R. G. HANSEN. *Pediatrics* [*Pediatrics*] **25**, 572–581, April, 1960. 5 figs., 28 refs.

Assay of galactose-1-phosphate uridyl transferase in erythrocytes has been applied to a study of 14 families in which a known case of galactosemia has occurred. Including normal controls, 278 individuals were involved. The method employed was sensitive enough to differentiate between homozygous, heterozygous and normal individuals.

The results substantiate the conclusion that galactosemia is a genetic disease transmitted by simple autosomal Mendelian inheritance.—[Authors' summary.]

Public Health and Industrial Medicine

1318. **" Premature " Children at Primary Schools**
J. W. B. DOUGLAS. *British Medical Journal* [*Brit. med. J.*] **1**, 1008–1013, April 2, 1960. 4 refs.

The study herein reported from the University of Edinburgh is a continuation of an earlier one (*Brit. med. J.*, 1956, **1**, 1210; *Abstr. Wld Med.*, 1956, **20**, 319) in which the author assessed the mental ability of 8-year-old children who had been born prematurely. The mental ability tests were repeated in the same groups of children when they were 11 years of age and attending normal primary schools, and the results together with those of the " 11+ " (secondary school selection) examination and the teachers' comments are now analysed. Of the original 675 children 408 completed all the tests at 8 years and 355 at 11 years. In all respects the children who had been prematurely born fared less well than controls. Further, the comments of the teachers on their powers of concentration, attitude to work, and discipline were unfavourable, compared with controls. Only 9·7% obtained a place in a grammar school, compared with 22% of the controls. These differences were due not to school absences, but largely to adverse home conditions, particularly lack of parental care and interest in the child's educational progress. The author discusses the difficulty of long-term control studies, and points out that a control group which is satisfactory at the beginning of a longitudinal inquiry is not necessarily satisfactory at the end. *R. S. Illingworth*

1319. **Relation between Mortality from Cardiovascular Disease and Treated Water Supplies: Variations in States and 163 Largest Municipalities of the United States**
H. A. SCHROEDER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 1902–1908, April 23, 1960. 10 refs.

Death rates from cardiovascular causes in the United States vary widely from State to State. In 1949–51 degenerative heart conditions, including coronary disease, accounted for about 22% of all deaths, about 43% of all deaths from cardiovascular disease, and about 50% of cardiovascular deaths in males. Extreme rates (in males) were 336 per 100,000 in New York and 148 in New Mexico. These variations have not been explained on the basis of dietary habits, racial background, or environmental stresses and strains. One variable environmental influence to which all populations are exposed is drinking water, and the present author reports a large scale study of death rates by State for the years 1949 to 1951 and the results of an analysis of certain properties of public water supplies. Significant negative correlations were found between mean hardness of water and mortality from all causes, from cardiovascular diseases, and, in males, from coronary heart disease and all other cardiovascular diseases; there was no correlation between hardness of water and non-cardiovascular deaths. There were highly significant negative correlations between hardness of water and deaths from cardiovascular diseases, coronary heart disease, and other cardiovascular causes in white males aged 45 to 64 years; no correlation was observed between hardness of water and mortality from non-cardiovascular disorders in this group. In all cases the correlations were negative—that is, softer water was associated with higher death rates.

Analysis of total death rates and mortality from coronary heart disease in white men aged 45 to 64 years in the 163 largest cities again showed highly significant negative correlations with total water hardness. Estimation of 20 constituents of municipal water for each city and analysis of certain characteristics of the water revealed highly significant correlations with the contents of magnesium, calcium, bicarbonate, sulphate, fluoride, and dissolved solids, and with the specific conductivity of water and its *p*H, higher values of all these again being associated with lower death rates.

The author concludes that some factor either present in hard water or missing from soft water appears to affect the death rates. " The data offer a clue to an environmental influence associated with the nature of public water supplies which affects adversely the course of degenerative cardiovascular diseases in the United States." *A. J. Karlish*

1320. **Atmospheric Pollution in City Streets by Motor Vehicles Using Ethyl Petrol.** (Загрязнение воздуха улиц городов автотранспортом ври применении этилированного бензина)
F. I. DUBROVSKAJA. *Гигиена и Санитария* [*Gig. i Sanit.*] **25**, 15–18, April, 1960. 2 figs., 6 refs.

The amount of lead discharged into the atmosphere from the exhaust of motor vehicles increases with increase in the speed of the vehicle. Thus an idling engine was found to emit 0·3 g. of lead for each kg. of petrol consumed, but when travelling at 40 km. per hour this value increased to 0·9 g. per kg. Investigations were carried out in 5 towns in the U.S.S.R. in order to ascertain the degree of atmospheric pollution by inorganic lead compounds produced by the combustion of ethyl petrol in motor vehicles. By using a pipe from the air inlet of the carburettor of a motor lorry as an aspiration pump samples of air ranging in volume from 14·4 to 18 cubic metres were collected in streets away from possible industrial sources of pollution with lead. The lead in the air samples was then estimated by conversion to lead sulphate with sulphuric acid at 500° C., and further conversion via lead acetate to lead chromate. The concentrations of lead in the air were found to vary from 0·03 to 15 μg. per c. metre. Higher values were obtained in towns where ethyl petrol was in use, and the concentration of lead was also higher during the daytime than at night. The accepted maximum permitted concentration of lead in working places (0·7 μg. per c. metre) was exceeded at most of the sampling points.

Investigations of the state of health of traffic police revealed evidence of vegetative nervous dysfunction, this being especially marked in men stationed where lead concentrations were high, while examination of the blood showed reticulocytosis and punctate basophilia. One traffic controller had to be admitted to hospital for treatment of lead poisoning, although he had been in contact with no other source of lead. *Basil Haigh*

1321. **Control of Staphylococcal Food Poisoning**
B. E. HODGE. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] **75**, 355–361, April, 1960. 17 refs.

The author has reviewed 95 outbreaks of staphylococcal food poisoning reported to the U.S. Public Health Service during 1955 and 1956. The diagnoses were based on the opinions of the reporting medical officers of health and on the presence of staphylococci found in the incriminated food, these organisms being typed and the incubation periods of the illness also taken into account, since there are no reliable laboratory tests for staphylococcus enterotoxin and for enterotoxigenicity of the strain isolated.

In 94 (99%) of the outbreaks the vehicle incriminated was a cooked food or a food mixture which was rich in protein and had undergone a certain amount of handling after heat treatment or other preparation. Instead of being adequately chilled within a short time these foods had been kept warm or at room temperature for 4 hours or longer, thus allowing the contained organisms to multiply, with consequent production of enterotoxin in the interval. Left-over food was the vehicle incriminated in 81 (94%) of 86 outbreaks. Infections present in those handling the food, insanitary practices on the part of the latter, or faulty environmental conditions did not figure prominently among the circumstances associated with these outbreaks.

The techniques of manufacture, cooling, and keeping of foods would seem to be the overwhelmingly important factor in the prevention of staphylococcal food poisoning. It is recommended that shallow containers should be used for the cooking or other heating and for chilling of protein-rich foods and they should never be kept at a temperature above 40° F. (4·5° C.) for more than an aggregate of 3 hours. The insulating effect of, for example, pastry or bread as in éclairs, patties or sandwiches, on its protein-rich enclosures, should not be overlooked, and these articles should either be freshly prepared or if suitable reheated to at least 150° F. (66° C.).
J. Cauchi

1322. **Epidemic Control of Poliomyelitis with Inactive Virus Vaccines: Studies in Cynomolgus Monkeys**
D. S. DANE, G. W. A. DICK, J. J. MCALISTER, and R. T. NELSON. *Lancet* [*Lancet*] **1**, 845–849, April 16, 1960. 5 figs., 11 refs.

In man 80 to 90% protection against paralytic poliomyelitis can be conferred by 2 or 3 doses of 1 ml. of the inactivated poliovirus vaccines in present use, but one dose confers no obvious protection during the weeks following inoculation. The authors report from the Queen's University, Belfast, the results of inoculating cynomolgus monkeys with a single dose of 10 ml. of commercial vaccine and a week later challenging the animals with an intracardiac inoculation of virulent Type-1 virus of the Barr strain. Of the 11 pairs of adult monkeys observed one from each comparable pair was allocated to the vaccination group and the other to the control group. One week after vaccination 8 of the 11 vaccinated animals had developed low titre Type-1 neutralizing antibody, and of these 7 remained in good health after the challenge, but the 8th monkey and the 3 which failed to develop detectable neutralizing antibodies became paralysed 7 to 17 days after the challenge. In the control group 9 of the 11 monkeys became paralysed. Viraemia, which was found only in the monkeys which became paralysed, lasted 2 to 6 days.

Type-1 poliovirus was isolated from the faeces on only 2 occasions from 2 monkeys, but the virus was isolated from the throat of 11 of the 13 animals with viraemia for 2 to 8 days, usually from the day after the detection of the viraemia. In the monkeys which remained healthy serum antibody titres 7 weeks after vaccination were less than 1:4 in all but one; this animal had a titre of 1:45, even though virus was never recovered from it. These results indicate that a single dose of 10 ml. of inactivated vaccine may be useful in protecting man in an epidemic. They also suggest that throat virus may be equally important in the dissemination of poliomyelitis in man.
A. Ackroyd

1323. **Response of Cuban Children to Oral Vaccination with Living Attenuated Poliovirus Vaccines: a Clinical and Serological Study**
J. EMBIL JR. *British Medical Journal* [*Brit. med. J.*] **1**, 1157–1162, April 16, 1960. 1 fig., 5 refs.

Writing from the Municipal Children's Hospital, Havana, the author states that by the age of 9 years at least 75% of the children in Cuba possess antibodies to all three types of poliomyelitis virus, but paralytic poliomyelitis does occur as a sporadic disease in early childhood, with periodic relatively small outbreaks. Because the social and economic conditions in Cuba make the use of the Salk-type vaccine difficult, the author and collaborators carried out a series of trials with the Lederle oral attenuated poliovirus vaccines under varying conditions among groups of children, mostly 5 to 12 years old, residing in orphanages, dormitory schools, or temporarily in recreation camps. Among some 2,000 subjects who have so far received these vaccines no clinical evidence of nervous or other disturbances attributable to the vaccines have been observed and the vaccination by this method of children who subsequently developed an acute infectious disease, such as mumps, rubella, or influenza, or who had certain chronic diseases, has produced no adverse reactions nor aggravated the infectious disease.

Serological results in 526 children divided into six groups of varying size showed some differences in conversion rates from sero-negative to sero-positive as between groups and virus types, but the over-all rate was 88%. Fourfold booster responses occurred in the children whose pre-vaccination antibody titres were be-

tween 1:4 and 1:512 to the extent of 36% of 329 children against virus of Type 1, 45% of 287 for Type 2, and 62% of 328 for Type 3. The mean titres showed that gains in antibody titres for Type-2 virus were in general less marked than for Types 1 and 3. In Group 1, 16 children were given capsules containing virus at intervals of 3 weeks, the order being Type 2, Type 1, and Type 3, washed down with one of the popular highly carbonated beverages; no inhibitory action by the high acidity of this beverage was evident, the conversion rate being 83% and fourfold booster responses were frequent. To Group 2 (62 girls) one capsule each of virus Types 1 and 3 and two of virus Type 2 were given simultaneously together with a suspension of non-fat milk solids to facilitate swallowing; the conversion rate for the 36 children who were sero-negative before taking the vaccine was 89%. In Groups 3 and 5, 96% and 94·7% respectively of the 23 and 38 sero-negative children converted to positive when the viruses were fed at weekly intervals in the order Types 2, 3, and 1. In Group 4 contact spread was not observed when 87 of 105 children in a home for foundlings, most of whom had received Salk vaccine, were given the virus at intervals of 4 to 5 weeks in the order Types 2, 3, and 1, but the conversion rate was only 67% among the 12 sero-negative children. In Group 6 consisting of 159 children in similar circumstances to those in Group 4 but who received the vaccines at weekly intervals, the conversion rate was 80%.

It is considered that the high response rate to all 3 types of virus given simultaneously is a finding of great practical importance, and its implications are discussed.

A Ackroyd

1324. **Trial of Adenovirus Vaccine in Royal Air Force Recruits**

J. S. Wilson, P. J. Grant, D. L. Miller, C. E. D. Taylor, and J. C. McDonald. *British Medical Journal* [*Brit. med. J.*] **1**, 1081–1083, April 9, 1960. 12 refs.

It has been demonstrated in several large field trials in the United States that adenovirus vaccines are effective against acute respiratory disease due to these viruses. Since in the R.A.F. the principal cause of discharge because of respiratory disease was a respiratory illness acquired during recruit training, inoculation of recruits with a commercial vaccine containing adenovirus Types 3, 4, and 7 was tried at the R.A.F. Station at Bridgnorth. Each week recruits on arrival were allocated to one of five flights of 70 to 80 men. During February, 1959, 91% of the strength of two incoming flights each week were inoculated. Most of the 402 recruits received the injection within 24 hours of arrival, and the remainder within 48 hours. Clinical record cards were completed for every recruit admitted to sick-quarters or to hospital until the end of March, and material was taken for virus isolation and for serological examination. It was found that influenza A and B and adenovirus infections, especially Type 3, were prevalent before and during the trial. The effect of the vaccine was to reduce by 40% the admission rate for acute respiratory illness occurring more than one week after inoculation. The protection afforded against adenovirus infections, as estimated from the results of virus isolation, was 70%. Mild local and general reactions to the vaccine were observed in less than 10% of the inoculated men.

J. E. M. Whitehead

INDUSTRIAL MEDICINE

1325. **Biochemical Experiments on the Binding of Chrome to Skin**

F. E. Anderson. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 149–157, April, 1960. 16 refs.

It is widely held that the production of allergy by simple chemicals such as chromium and nickel is the result of the binding of these substances with a protein molecule derived from epidermis or dermis to form the stimulating allergen. From the results of experiments with nickel Wells (*Brit. J. Derm.*, 1956, **68**, 237; *Abstr. Wld Med.*, 1957, **21**, 55) considered that the carboxyl group of the horny layer might play a part in nickel binding. In the present investigation, carried out at the Royal Victoria Hospital and Queen's University, Belfast, somewhat similar experiments were performed with chromium. Specimens of skin freshly excised or obtained at necropsy were placed in a potassium chromate bath for 2 hours, the specimen being then washed for 12 hours, dried, and weighed. All chromium was oxidized to the hexavalent form, the Kjehdahl apparatus being used, diphenylcarbazide was added, and colorimetric readings were taken. Various methods were employed to block certain radicals, including sulphydryl (SH) blocking by iodoacetamide, SH release by sodium sulphite, deamination with Van Slyke's nitrous-acid reagent, methylation, benzoylation, and extraction of lipids. Only methylation and benzoylation resulted in an increased uptake of chromium from the dichromate bath.

Several interesting side-results were observed. The trivalent form of chromium is more readily absorbed than is the hexavalent, yet collagen, which, in the opinion of many workers, holds the chromium, behaves in exactly the reverse fashion. The skin also shows an increased uptake of chromium at acid *p*H; this, the author points out, is pertinent to the work in the leather tanning industry, but cannot be related to the situation in the cement industry where an alkaline *p*H is important. Apparently the production of dermatitis is not quantitatively related to the amount of chromium taken into the skin in the cement industry, but is of more importance in tanning, in which trivalent chromium is concerned. By a process of elimination it would appear that amino groups, sulphydryl groups, and hydroxyl radicals are not involved, and that the major part of the binding is done by freed carboxyl groups, possibly made available by the presence of associated chemicals. *Allene Scott*

1326. **Smoking Habits Related to Injury and Absenteeism in Industry**

C. R. Lowe. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **14**, 57–63, April [received July], 1960. 6 figs., 4 refs.

A study is reported from the University of Birmingham of the smoking habits in relation to absenteeism and to the frequency of attendance for treatment of injury in

a group of 3,341 male workers for whom, out of a total of 7,680 employees of an industrial concern, information was available for the 12-month period ending December, 1957. Of the 3,341, 777 (23·3%) had never smoked and 280 (8·4%) had given up smoking. Of the remainder, 158 (4·7%) smoked a pipe only, 361 (10·8%) smoked up to 10 cigarettes a day, 988 (29·6%) smoked between 10 and 20, 604 (18·1%) between 20 and 30, and 173 (5·2%) more than 30. Absenteeism for non-medical reasons appeared to be unrelated to smoking habits. On the other hand, absenteeism for medical reasons and the frequency of attendance for treatment of injury were both higher in smokers than in non-smokers and increased fairly regularly with the amount smoked. The relationship between smoking and injury was more pronounced among younger men while that between smoking and absenteeism was more marked in older men. The mean number of injuries treated per worker in non-smokers under 25 years of age was 1·23, whereas in those in the same age group smoking more than 30 cigarettes a day it was 2·75. For all age groups the number of injuries treated per worker in non-smokers was 1·05 and in those who smoked more than 30 cigarettes a day it was 1·54. The number of days absent for medical reasons per worker in non-smokers was 5·49, in those smoking between 10 and 20 cigarettes 6·2, and in those who smoked over 30 cigarettes 8·63. Days absent per worker for non-medical reasons averaged 4·32 in non-smokers, 4·34 in those smoking between 10 and 20 cigarettes, and 4·52 in those smoking over 30.

The author states that although it is conceivable that smoking has some pharmacological effect upon muscular co-ordination, it seems more likely that young people who smoke heavily are temperamentally more accident prone than those who are light smokers or non-smokers. While there may well be a genetic link between smoking and accident, it is most unlikely that smoking, lung cancer, chronic bronchitis, coronary arterial disease, peptic ulcer, and respiratory tuberculosis, are linked through genetic susceptibility. *Kenneth M. A. Perry*

1327. **An Experimental Investigation into the Action of Dust of Ore Concentrates of Rare Metals on the Lungs.** (Экспериментальное исследование действия пыли концентратов руд редких металлов (пылевых смесей))

O. Ja. Mogilevskaja. *Гигиена и Санитария* [*Gig. i Sanit.*] **25**, 30–35, April, 1960. 3 figs., 5 refs.

The effect on the lungs of rats of the experimental injection of a dust of the ores of the following rare metals was investigated: a molybdenum concentrate containing 94·5% molybdenum sulphide and 5·5% free silicate, a titanium concentrate containing 54·7% titanium oxide, 38·7%, iron oxide, and 2·2% free silicate; and a beryllium concentrate containing 90% of beryllium and other oxides and 10% free silicate. The dust was given by intratracheal injection as a suspension of 50 mg. in 0·6 ml. of physiological saline solution.

The animals, which were killed after 5 to 7 months, all showed a decreased gain in weight compared with controls. The effects of the dust on the lungs differed with each metal. Thus the dust of the beryllium concentrate caused diffuse fibrosis of the lungs together with a focal production of lesions containing dust particles, fibroblasts, histiocytes, and connective tissue fibres which developed up to 5 months after inhalation of the dust. Miliary nodules of epithelioid cells affected the regional lymph nodes. The molybdenum concentrate caused a moderate diffuse fibrosis of the lungs after 7 months, and a late development of lesions in the regional lymph nodes. The reaction to titanium dust was even less pronounced, and the lymph nodes were practically unaffected. The conclusion reached is that the dust from mixed ores may have a more pronounced action on the lungs than that from one rare metal alone.

Basil Haigh

1328. **Methods of Study of the Incidence of Pneumoconiosis.** (О методах изучения заболеваемости пневмокониозами)

E. V. Huhrina. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **4**, 7–13, April, 1960.

In comparing the statistics from different centres or different countries in respect of the incidence of pneumoconiosis difficulties are encountered because of lack of uniformity of the criteria of assessment of the disease. In this paper the author analyses reported figures for the incidence of pneumoconiosis among workers in different industries in several countries, and on the basis of this analysis he recommends that in the presentation of statistical data on this subject the information given should include: (1) the number of new cases per annum per 100 workers examined, together with the duration of exposure at work in 5-year periods, 0 to 5, 6 to 10, 11 to 15, and so on; (2) the average length of time at work of those in whom Stage-1 pneumoconiosis was first diagnosed during the year; (3) the average age of those developing Stage-1 pneumoconiosis in the year; (4) the average length of working life and average age of those dying from pneumoconiosis during the year.

Statistics relating to persons suffering from complicated pneumoconiosis (associated with tuberculosis) should be given separately. Such statistics of the incidence of pneumoconiosis should also always be accompanied by data on the working conditions and the dust concentrations to which workers are exposed so as to enable preventive measures to be evaluated and limits established for maximum permissible concentrations of dust in the working atmosphere. *Basil Haigh*

1329. **Dust Content, Radiology, and Pathology in Simple Pneumoconiosis of Coalworkers. Part I: General Observations. Part II: Detailed Analysis of the Data**

D. Rivers, M. E. Wise, E. J. King, and G. Nagelschmidt. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **17**, 87–108, April [received June], 1960. 13 figs., 21 refs.

This paper, the result of combined studies carried out at the Pneumoconiosis Research Unit, Llandough, Glamorgan, the Postgraduate Medical School of London, and the Safety in Mines Research Establishment,

Sheffield, describes a study of the radiological changes during life of simple pneumoconiosis in 45 coal-workers and in their lungs examined subsequently at necropsy. Cases of complicated pneumoconiosis were not included. Since the bodies of miners coming to necropsy in hospital would probably provide a biased sample the post-mortem material was taken from men killed in pit accidents and to make up sufficient numbers from coal-workers coming to necropsy at the Welsh National School of Medicine. The main criteria in the choice of material were absence of tumour, tuberculosis, and gross discrepancies between right and left lung, and of course the availability of recent chest radiographs, that is, within 2 years of death. Of the 45 cases in all collected between 1952 and 1955 13 were derived from pit accidents.

In each case the left lung, prepared by the large-section technique of Gough and Wentworth, and the right, sliced sagitally, were examined by two pathologists. Blocks from the two lungs were subjected to standard histological methods, and treated respectively with reticulin and collagen stains, quantitive grades for reticulin and collagen being laid down. Dust analyses were carried out only on the right lungs (excluding lymph nodes) after they had been dried at 105° C., weighed, and ground. Coal, total silica, and quartz contents were estimated in two laboratories and the results found to be in good agreement. Chest radiographs were examined and classified in 4 categories (without foreknowledge of the cases) by two independent pairs of " readers " and then by all four readers together, the International Labour Office Classification of 1950 being used.

The value for total dust in the right lung plotted against the radiological reading showed a clear increase in the average weight of total dust found with rising radiological category, though there was considerable overlapping between the categories. The fatal accident cases did not appear to differ substantially from the others. The ranges of dust content for the 4 radiological Categories 0, 1, 2, and 3 were respectively 1·4 to 14·2 g., 5·3 to 19·2 g., 4·5 to 30·8 g., and 17·0 to 44·1 g. The average amount of dust in one lung of a miner in radiological Category 0 was observed to be about 10 times greater than the average amount previously reported in the lungs of adult town dwellers. Larger amounts of reticulin tended to occur in association with increasing radiological category and a slight trend for increased quantities of collagen went hand in hand with this. Age was not an important variable influencing the rate of dust retention. The hypothesis that the degree of radiological change in the lungs depends only upon the *total* weight of dust in the lungs was not confirmed on analysis of the data. One gramme of silicates was found to contribute approximately the same amount to the radiological changes as 9 g. of coal, and the authors suggest that this may depend upon the unequal absorption of x rays by the two substances, rather than upon a " biological " explanation, in that such an explanation was found to be inconsistent with the observed low-grade tissue reaction to the dust and the poor correlation of periods of dust retention with radiological change. Hence, the authors' conclusion is that it is the quantity of mineral dust in the lungs of coal-workers with simple pneumoconiosis which is responsible for the radiological changes rather than tissue reaction.

The second part of the paper is devoted to a more detailed, and partly mathematical, analysis of the following aspects of the problem: factors other than total dust affecting radiological change; contribution to radiological changes of carbon and mineral content; periods of dust retention and estimation of amount of progressive tissue reaction; reticulin, collagen and fibrous dust nodules; difference in the absorption of x-rays between carbon and minerals; and the influence of electron voltage of the x rays on their absorption.

[This paper is of the utmost importance as a contribution to the problem of correlation of the radiological appearances in the lungs during life with findings in the lungs at death in coalworkers' pneumoconiosis, and should be read in full by all interested.]

W. Raymond Parkes

1330. **Pneumoconiosis in Makers of Artificial Grinding Wheels, Including a Case of Caplan's Syndrome**
E. Posner. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **17**, 109–113, April [received June], 1960. 3 figs., 38 refs.

Up to the third decade of the present century cutlery and other metal grinders in the United Kingdom suffered a high rate of pneumoconiosis as a result of working with grinding wheels made of natural sandstone. In the last 30 years this material was gradually replaced by carborundum (silicon carbide) and corundum (aluminium oxide) with a consequent reduction in the incidence of metal grinders' pneumoconiosis. However, those who manufacture the newer grinding wheels and fire the ceramic vitrified bond materials are themselves open to the risk of pneumoconiosis, and possibly these materials may be more active in this respect than carborundum.

At the Mass Radiography Centre, Stoke-on-Trent, the author has examined radiologically 42 men working in a " bond " preparing and mixing department where the wheels are made and fired. The radiographs were examined by two groups of independent observers and their results were in close agreement. Of 17 of the men showing radiological evidence of pneumoconiosis, " nodular " opacities being mainly of the silicotic type, 6 also had progressive massive fibrosis. In 2 men who later died necropsy revealed classic silicosis with progressive massive fibrosis. In another man with rheumatoid arthritis chest radiographs showed appearances typical of rheumatoid pulmonary disease of nodular form.

The ceramic vitrified " bond " which is used to hold together abrasive grains within the grinding wheel appears to consist mainly of various mixtures of felspar, ball clay, and silica and although these contain considerable quantities of silica, measures are now being taken to reduce the amount of dust inhaled by the man on this work. Nevertheless the manufacture of carborundum and corundum wheels may offer some risk, and the possibility also exists of pneumoconiosis occurring in those who use such wheels.

[The value of this paper lies in drawing attention to an industrial risk which is not widely recognized.]

W. Raymond Parkes

Anaesthetics

1331. **Trimeprazine Tartrate in Paediatric Premedication: a Preliminary Communication**
G. B. GILLETT and A. M. KEIL. *Anaesthesia* [*Anaesthesia*] **15**, 158–162, April, 1960. 2 refs.

Trimeprazine tartrate, a phenothiazine derivative, was given for premedication to about 150 children, aged 16 months to 12 years, most of whom were undergoing ear, nose, and throat operations at St. Bartholomew's Hospital, London. It was administered in the form of a syrup (vallergan forte) in a dose usually of 1·5 mg. per lb. (3·3 mg. per kg.) body weight. Most of the patients were also given 0·6 mg. of atropine and some received 0·2 mg. of scopolamine one hour before operation. Trimeprazine was most effective if given 2 hours or more before operation. Nearly all the children went to sleep in the ward, especially if they had received scopolamine. After operation many slept for several hours. The incidence of postoperative vomiting was reduced.

Mark Swerdlow

1332. **Endotracheal Intubation: Effects on Blood Pressure and Pulse Rate**
C. C. WYCOFF. *Anesthesiology* [*Anesthesiology*] **21**, 153–158, March–April, 1960. 3 figs., 4 refs.

In 1951 King *et al.* reported a marked though transient rise in blood pressure during performance of endotracheal intubation. In the present study, carried out at the Presbyterian Hospital, New York, intra-arterial blood pressures and pulse rates were recorded in 25 patients subjected to endotracheal intubation on 34 occasions. They were divided into three roughly equal groups in which intubation was performed respectively with surface anaesthesia only, with succinylcholine chloride only, and with a combination of both procedures. Light thiopentone anaesthesia was used in all three groups. In Group 1 the blood pressure rose in all cases on laryngoscopy; in Group 2 there was also a rise, which though transient was significantly greater than in Group 1.

W. Stanley Sykes

1333. **Rediscovery of Air for Anaesthesia in Thoracic Surgery**
H. F. POPPELBAUM. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **53**, 289–294, April, 1960. 9 figs.

The author describes a simple double-bellows non-rebreathing apparatus for inflating the lungs with air during anaesthesia for thoracic surgery. In patients undergoing operation at the Tuberculosis Research Institute, Berlin–Buch, premedication with promethazine (50 mg.), pethidine (100 mg.), and atropine (0·6 mg.) was followed by induction of anaesthesia with an intravenous barbiturate, and a relaxant to facilitate intubation, with maintenance by ether in air (up to 5%) and curare as required. In 100 cases the oxygen saturation of the blood was measured with an oximeter, and the respiration of each lung measured by pneumotachographs attached to each of the two limbs of a Carlen's tube. Under normal conditions the oxygen saturation was arbitrarily assumed to be 80% for a patient breathing air, since no absolute figures were obtainable without full saturation with oxygen-rich mixtures. Temporary falls in saturation occurred during intubation, and on first permitting spontaneous respiration at the end of the operation.

A method of broncho-oximetry is also described, in which the lung to be resected is filled with nitrogen, while the patient breathes air with the normal lung; if there was no appreciable fall in blood oxygen saturation, pneumonectomy was considered possible; otherwise, a limited resection only was advised. A similar test was carried out on anaesthetized patients. It is not claimed that added oxygen should not be used, but that it is not essential for such procedures, notably in situations where heavy cylinders of compressed gases cannot be made available. It is recalled that ether in concentrations of 5% or less in air is inflammable, but not explosive.

D. D. C. Howat

1334. **Anaesthesia for Intracardiac Surgery Using Cardiopulmonary Bypass**
P. M. LUMB. *Anaesthesia* [*Anaesthesia*] **15**, 163–171, April, 1960. 3 figs., 26 refs.

The author describes the anaesthetic technique employed at the Queen Elizabeth Hospital, Birmingham, in 20 cases of open-heart operation. Endotracheal nitrous-oxide–oxygen anaesthesia with curare is used in closed circuit with controlled respiration. The heart is bypassed and arrested, the body circulation being maintained by a pump oxygenator. Full details are given of the management of anaesthesia and the circulation, and the results are compared with those reported by other workers. The author emphasizes the importance of accurate correction of blood loss and the value of continuous electroencephalography. *Mark Swerdlow*

1335. **The Protective Effect of Anaesthesia on Experimental Renal Ischaemia**
H. L. SHEEHAN and J. C. DAVIS. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **79**, 337–345, 1960. 2 figs., 12 refs.

Experiments were carried out in the Department of Pathology, University of Liverpool, to determine whether pre-treatment with prolonged general anaesthesia protects the kidney from the effects of ischaemia. Prolonged general anaesthesia was given to 39 rabbits and various other drugs to 30. The anaesthetic was administered continuously for 2 hours before applying the renal pedicle clamps. An intravenous injection of 60 mg. of pento-

barbitone 2 to 3 hours before the pedicle was clamped was followed by intermittent small injections to keep the animals unconscious and maintain a respiratory rate of 6 to 12 per minute. A further small dose of 20 mg. of " nembutal " was injected just before removal of the clamps, to ensure that the first blood entering the kidney contained nembutal. In a second set of experiments the animals were deeply anaesthetized with ether given by an open mask; in a third set ethylurethane was injected intravenously in a 20% solution, most of these animals being given 3 to 6 ml. just before the removal of the clamps.

There was much less necrosis of the proximal tubules in the animals given prolonged anaesthesia than in controls. The latter had very extensive necrosis after 1½ hours of ischaemia, whereas after long anaesthesia the proximal tubules showed no necrosis after 1½ hours, some degree of necrosis at 3 hours, and severe necrosis at 4 hours. Prolonged anaesthesia greatly facilitated the re-establishment of circulation through the kidney. With long anaesthesia the ischaemia can be continued for 2½ to 3 hours with a good prospect of obtaining reflow through the medulla, and for 4 hours as regards a reflow through the cortex. The sensitivity of glomeruli to ischaemia was reduced by prolonged anaesthesia, as shown by the lower incidence of necrosis and thrombosis in the glomerular tufts when clamping for 2 hours was carried out under long anaesthesia. There was little indication that long anaesthesia influenced the occurrence of capillary aneurysms in the tufts or had any protective effect on the arteries. *M. Woods*

1336. **Cyclopropane Arrhythmias in the Cat: Their Cause, Prevention and Correction**
B. H. Robbins and J. D. Thomas. *Anesthesiology* [*Anesthesiology*] **21**, 163–170, March–April, 1960. 6 figs., 10 refs.

The arrhythmias which are well known to occur during cyclopropane anaesthesia were studied at Vanderbilt University School of Medicine, Nashville, Tennessee, in cats, a species which is very susceptible to this phenomenon. It was shown that such arrhythmias could easily and regularly be produced by a mixture of 30 to 40% cyclopropane in oxygen. Normal rhythm could be restored by supplemental respiration, or by the intravenous infusion of barbiturates. It was also found that bilateral sympathectomy did not prevent the occurrence of ventricular arrhythmias in the cat.
W. Stanley Sykes

1337. **Hyperventilation with Oxygen—a Possible Cause of Cerebral Hypoxia**
K. Sugioka and D. A. Davis. *Anesthesiology* [*Anesthesiology*] **21**, 135–143, March–April, 1960. 6 figs., bibliography.

It was shown by Kety and Schmidt (*Fed. Proc.*, 1946, **5**, 55) that active or passive hyperventilation caused a decrease in cerebral blood flow. It therefore occurred to the present authors that this in turn might cause cerebral hypoxia, even in the presence of increased oxygen saturation. In experimental studies on dogs, carried out at the University of North Carolina, in which they used the oxygen electrode (which is described), they found that, while breathing pure oxygen brought about a 90% rise in cerebral oxygen tension, hyperventilation with air or oxygen caused a fall in cerebral pO_2. The addition of carbon dioxide during hyperventilation, however, caused a dramatic rise in cerebral pO_2 so long as the CO_2 was being inhaled. Hyperventilation in anaesthesia may thus be harmful. *W. Stanley Sykes*

1338. **Prediction of Carbon Dioxide Tension during Anaesthesia**
J. F. Nunn. *Anaesthesia* [*Anaesthesia*] **15**, 123–133, April, 1960. 4 figs., 16 refs.

During spontaneous respiration, prediction of the arterial carbon dioxide tension of an anaesthetised patient is rendered very difficult by the unsteady respiratory state which is usually present. Radford's nomogram should still give a reliable guide of what is an adequate ventilation, but it should not be expected that a correlation will always be shown between the arterial carbon dioxide tension and the ventilation expressed as a percentage of standard. During artificial ventilation with the chest closed, prediction of carbon dioxide tension is reasonably satisfactory and there is fairly good correlation between the tension and the ventilation. Radford's nomogram should give a reliable indication of the correct ventilation. During thoracotomy there is poor correlation between carbon dioxide tension and ventilation, largely due to variation in the physiological dead space. Ventilation nomograms will be almost valueless in these circumstances and the arterial carbon dioxide can be ascertained only by direct measurement. —[From the author's summary.]

1339. **Induced Hypotension and Post-operative Bleeding**
I. C. K. Tough. *Anaesthesia* [*Anaesthesia*] **15**, 154–157, April, 1960. 13 refs.

The effect of induced hypotension on postoperative haemorrhage was studied at the City Hospital, Edinburgh, in 381 patients undergoing major thoracotomy. Controlled hypotension was employed during anaesthesia in 268 of the patients while the remaining 113 served as controls. Postoperative haemorrhage was considered to be " significant " when 30 oz. (840 ml.) or more of blood drained off in the first 48 hours after operation. This degree of blood loss occurred in the same proportion of cases whether hypotensive drugs were used or not. These results suggest that induced hypotension does not increase the risk of postoperative haemorrhage.
Mark Swerdlow

1340. **The Experimental and Clinical Use of Profound Hypothermia**
D. Benazon. *Anaesthesia* [*Anaesthesia*] **15**, 134–145, April, 1960. 8 figs., 6 refs.

After a very brief review of some of the literature on profound hypothermia the author describes his experience at Westminster Hospital, London, of the use of low temperatures to achieve prolonged periods of complete circulatory arrest. Temperatures in the region of

14° C. were maintained in 28 patients undergoing open heart surgery. The extracorporeal circulatory system employed permitted oxygenation of the blood by the patient's own lungs. The anaesthetic technique and the measures taken to control coagulation are described in detail, together with the management of cardiac irregularities and of other complications. The author believes that profound hypothermia is a safe and useful procedure in open cardiac surgery. *Mark Swerdlow*

1341. **Vomiting by Out-patients after Nitrous Oxide Anaesthesia**

R. I. BODMAN, H. J. V. MORTON, and E. T. THOMAS. *British Medical Journal* [*Brit. med. J.*] **1**, 1327–1330, April 30, 1960. 3 figs.

The incidence of vomiting after administration of nitrous oxide and oxygen was studied in the records of 3,000 consecutive out-patients to whom nitrous oxide was given at the Hillingdon Hospital, Uxbridge, Middlesex. None of the patients received premedication or supplementary drugs, and the same intermittent-flow apparatus was used in all. Analysis of the records showed that vomiting or retching occurred in 440 patients (14·7%), and that the incidence was higher in children than adults and increased with the duration of anaesthesia. Following such procedures as reduction of fractures and cauterization of warts the incidence of vomiting was four or five times higher than that following incision of abscesses. The authors suggest that these factors should be taken into account when assessing the influence of drugs or techniques on the vomiting rate. Potentially dangerous vomiting occurred in about 1 in 18 patients undergoing operations for injuries sustained the same day, in spite of an interval of over 4 hours between the last meal and administration of the anaesthetic. It is suggested that since an accident may prolong the emptying time of the stomach, administration of a general anaesthetic should be postponed until the next morning. If this delay is not acceptable, the risks of hypoxia occurring during emergence vomiting can be reduced by giving oxygen after the anaesthetic. *J. V. I. Young*

1342. **Postoperative Nausea and Vomiting. III. Evaluation of the Antiemetic Drugs Fluphenazine (Prolixin) and Promethazine (Phenergan) and Comparison with Triflupromazine (Vesprin) and Cyclizine (Marezine)**

J. W. BELLVILLE, W. S. HOWLAND, and I. D. J. BROSS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 1488–1493, April 2, 1960. 4 figs., 8 refs.

The comparative effect on postoperative nausea and vomiting of four anti-emetic drugs, "trifluprom azine" (fluopromazine), cyclizine, "fluphenazine", and promethazine, was studied in 3,454 patients at the Memorial Center for Cancer and Allied Diseases, New York, a double-blind technique being used. The patients were divided into 6 groups according to the type of anaesthesia used and the operation performed, and the test drug or placebo was administered by random selection in each group. A nurse gave 1 ml. of the unknown drug when the patient arrived in the recovery room and recorded incidence of nausea and vomiting half-hourly. The doses were as follows: 7·5 mg. of fluopromazine, 12·5 or 25 mg. of promethazine, 4 or 8 mg. of fluphenazine, or 50 or 100 mg. of cyclizine. An untreated control group was also studied.

There was no significant difference between the control group and the patients receiving a placebo in the incidence of nausea and vomiting, 17·5% and 18·5% respectively. Fluphenazine, promethazine, and fluopromazine all reduced the incidence of nausea and vomiting to less than 5%, the differences between the three not being significant. No significant difference was observed with the varying doses given. Degrees of postoperative sickness were graded, but no significant differences were noted between the placebo group and the groups given anti-emetic drugs in the severity of nausea and vomiting. Analysis of drug dosage showed a significant reduction in severity with increasing dosage of fluopromazine, but not with fluphenazine, cyclizine, or promethazine. Of those receiving fluopromazine and promethazine, 5% were still asleep after 2 hours, while all those given the placebo only were awake, but this effect was not seen with cyclizine or fluphenazine. There was no significant difference between the placebo group and the treated groups in regard to changes in blood pressure.

The authors state that the three phenothiazine drugs studied were effective anti-emetics, but that only with fluopromazine was the severity of nausea and vomiting reduced with the higher dosage. Promethazine and fluopromazine both prolonged sleeping time, but fluphenazine did not. Hypotension occurred only with fluopromazine and then only when the dosage was 15 or 30 mg. Extrapyramidal symptoms have been reported after administration of fluphenazine, but none occurred in this series. *Raymond Vale*

1343. **Postoperative Nausea and Vomiting. IV. Factors Related to Postoperative Nausea and Vomiting**

J. W. BELLVILLE, I. D. J. BROSS, and W. S. HOWLAND. *Anesthesiology* [*Anesthesiology*] **21**, 186–193, March–April, 1960. 2 figs., 7 refs.

At the Sloan-Kettering Institute, New York, the authors have analysed the records of 3,794 patients who had received various drugs as prophylaxis against postoperative nausea and vomiting. The condition was found to be much more common in women than in men. Phenothiazine was very effective in reducing postoperative vomiting, especially in men. Cyclopropane anaesthesia caused the highest rate, ether the next, and thiopentone–nitrous-oxide the lowest. Administration of anaesthetics by mask caused more vomiting than tracheal intubation, and hypotension was also a factor in causation. The incidence rate was found to rise with the duration of anaesthesia and also with its depth. Abdominal operations, inexperience on the part of the anaesthetist, and obesity in the patient were all associated with increased incidence.

The authors suggest that there is a relationship between the progesterone and/or gonadotrophin level in women and the incidence of nausea and vomiting and state that studies of the menstrual cycle and the effect of the menopause have confirmed this. *W. Stanley Sykes*

Radiology

EXPERIMENTAL

1344. **Changes in the Cerebral Circulation in Rabbits following Whole-body Irradiation with X-rays or Gamma Rays.** (Изменение кровообращения головного мозга пви тотальном воздействии иа организм животного ионизирующей радиации)
R. M. LJUBIMOVA-GERASIMOVA. *Медицинская Радиология* [*Med. Radiol.* (*Mosk.*)] **5**, 24–29, April, 1960. 3 figs., 4 refs.

Experiments are described in which rabbits were irradiated with a single dose of 1,000 r. of x rays or γ rays and the subsequent changes in the pial blood vessels observed by means of serial cerebral arteriography and also directly through "plexiglass" windows inserted into the cranium.

Each stage of the radiation sickness was characterized by definite circulatory disturbances, as follows. (1) Immediately after the irradiation there was a transient vasoconstriction, soon followed by gradual vasodilatation, which became stabilized at 24 hours after the irradiation, when it was manifested mainly by dilatation of the venous vascular system. (2) During the second stage the circulation became normal, but as the radiation sickness developed the vessels tended to contract more and more, becoming almost thread-like. This resulted in marked cerebral anaemia and death of the animal one or 2 days later. *A. Orley*

1345. **Functional Morphology of the Heart in Radiation Sickness.** (Функциональная-морфология сердца при лучевой болезни)
S. N. SERGEEV. *Архив Патологии* [*Arh. Patol.*] **22**, 29–33, No. 4, 1960. 2 figs., 27 refs.

In experiments on 77 rabbits the animals were given a single large dose of irradiation (1,000 r.) by means of a radiotherapeutic machine. This dose produced distinct morphological changes in the myocardium. The animals were divided into three groups. The 21 rabbits in the first group were subjected after irradiation to regular daily exercise on a treadmill to the point of obvious fatigue; in 11 of these animals which died within the first 2 weeks and in the others which were killed at this time pronounced degenerative changes, such as fatty infiltration and homogenization of the sarcoplasm with loss of striation, were observed in the myocardium. The 15 animals in the second group were similarly exercised for 10 to 15 days but in this case before irradiation, and of these only one died during the first 2 weeks, the remainder being then killed, when examination showed that fatty infiltration of the myocardium was absent and the protein degenerative changes were minimal. The 19 rabbits in Group 3 were exercised both before and after irradiation; here only one of the animals died, and that from natural causes, and again in the others the myocardial changes were minimal, as in Group 2. It is concluded that these results suggest that systematic physical exercise tends to protect the heart muscle against radiation injury. *A. Swan*

RADIODIAGNOSIS

1346. **Localization of Intracranial Lesions Using Radioactive Iodinated Human Serum Albumin and an Automatic Scanner**
G. A. B. COWAN, S. O. FEDORUK, W. H. FEINDEL, and J. G. STRATFORD. *Journal of the Canadian Association of Radiologists* [*J. Canad. Ass. Radiol.*] **11**, 15–22, March [received May], 1960. 15 figs., 6 refs.

The authors of this paper from the Saskatoon Cancer Clinic and the University of Saskatchewan describe an automatic brain-scanning device for the location of intracranial lesions, and describe the results obtained using radioactive iodinated human serum albumin in 281 patients over a period of 2½ years.

The scanner has two collimated scintillation counters which move opposite each other on either side of the head in a series of eight parasagittal arcs. The record makes clear both the distribution of radioactivity and the differences in counting rate as seen from opposite sides of the skull. Thus the scanner is different from devices previously described. Adults are given 400 microcuries of radioactive iodinated human serum albumin 24 hours before scanning, the thyroid uptake being blocked by "Lugol's iodine" (aqueous solution of iodine). The patient wears a bathing cap to present a smooth uniform surface, and the head is fixed by cushioned clamps.

The results of scans were correctly correlated in 104 (90%) out of 115 cases in which the diagnosis was later verified by other methods. Of 166 unverified cases the results were inadequate for classification in 26. It is suggested that the method is simple, rapid, and of value as a screening procedure and better than most others in which manual scanning is used.
K. E. Halnan

1347. **Improved Visualization of the Ventricular System with the Technic of Autotomography**
M. M. SCHECHTER and BAO-SHAN JING. *Radiology* [*Radiology*] **74**, 593–600, April, 1960. 14 figs., 3 refs.

Autotomography was first described by Vallebona in 1930, but very few radiologists are aware of the detail and definition to be obtained from this procedure. The method is based on the fact that if the patient's head is rotated during an exposure while the tube and film are stationary, the radiographic image will be blurred except for structures at the axis of rotation. This principle has been applied in cerebral pneumography at St. Vincent's

Hospital, New York, where it was found to be especially useful in demonstrating the 4th ventricle, the iter, and 3rd ventricle. The use of this method reduces the need for positive contrast media.

The procedure is simple. During encephalography the patient rotates his head about 10 degrees, as though saying "No", during the exposure of the erect lateral views of the 4th ventricle. If he is unable to co-operate, his head is supported by a harness and passively rotated by an assistant. Similar rotation is carried out by a gloved assistant in the hanging-head and brow-down positions while the lateral radiographs are taken.

D. E. Fletcher

1348. **Frontal Avascularity: an Angiographic Observation in Frontal Lobe Tumors**

E. H. FEIRING, J. H. SHAPIRO, and A. I. FELDMAN. *Radiology* [*Radiology*] **74**, 601–604, April, 1960. 8 figs., 4 refs.

This paper from the Montefiore Hospital and New York University College of Medicine reports a study of the angiograms obtained in 41 cases of frontal-lobe tumour. In addition to the usual signs of vascular displacement and tumour filling the angiograms also demonstrated venous avascularity of the frontal region in 27 of the cases. This phenomenon, the cause of which is not known, may be of value in diagnosis where the anterior cerebral artery does not fill. *D. E. Fletcher*

1349. **Radiography by Means of a Tullium Preparation.** (Радиография с помощью препарата туллия)

V. V. ZODIEV, V. V. DMOHOVSKIJ, and L. A. MASLOV. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] **35**, 62–67, March–April, 1960. 3 figs., 2 refs.

Radioactive tullium (^{170}Tu) was used by the authors as a source of radiation for radiographic purposes. In view of the weakness of the source of radiation, however, intensifying screens had to be used, but even with the help of these the exposures had to be prolonged (from 7 to 70 seconds). This fact, in combination with a relatively large focal area (over 5 mm. in diameter), resulted in rather blurred radiographic images, bone structure in particular being indistinct. However the radiographic quality was adequate for the demonstration of radio-opaque foreign bodies and of gross fractures of bone. The apparatus proved unsuitable for use with image intensifiers.

The authors consider, however, that the apparatus could be perfected and ultimately compete with the standard x-ray generators. *A. Orley*

1350. **The Cinefluorographic Detection and Recording of Calcifications within the Heart**

J. JORGENS, N. BLANK, and W. A. WILCOX. *Radiology* [*Radiology*] **74**, 550–554, April, 1960. 6 figs., 9 refs.

The demonstration of small areas of intracardiac calcification on plain radiographs can be most difficult, while tomography and kymography have definite limitations for this purpose. Cinefluorography appears to be the method of choice and has been used in 803 examinations at the Veterans Administration Hospital, Minneapolis. Calcification was demonstrated in the left coronary artery in 225 cases, in the right coronary artery in 58, and both arteries in 38. Numerous valve calcifications were also seen.

A commercial apparatus, "cinefluorex", was used with a field diameter of 4·75 inches (12 cm.), run at 110 kV. and 5 to 15 mA. Radiographs were taken of the heart borders in the postero-anterior, the left and the right anterior oblique, and the right lateral projections, and of the mid-cardiac mass in the left anterior oblique position. At 15 frames per second 30 to 40 feet (9 to 12 m.) of film were used in each examination, and the total skin dose given to each patient was about 20 r. in air. *D. E. Fletcher*

1351. **Arteriography in the Diagnosis of Dissecting Aneurysm**

D. SUTTON. *Clinical Radiology* [*Clin. Radiol.*] **11**, 85–92, April, 1960. 11 figs., 16 refs.

Dissecting aneurysms most commonly involve the thoracic aorta, but cases of more peripheral involvement have been described and 2 are reported in this paper from St. Mary's Hospital, London.

About two-thirds of the patients with dissecting aneurysm are hypertensive. Clinically, severe pain is a constant feature and the heart rhythm may be abnormal. Other signs depend on whether the main vascular branches of the aorta are occluded by the aneurysm. Some 80% of patients die within 4 days of the onset; in the few who survive the aneurysm becomes chronic. Radiologically, the diagnosis may be suggested from the plain radiograph of the chest; this is more certain in a patient who is known to have recently had a normal mediastinal shadow but who now presents with a gross widening of the ascending or descending aorta. Arteriography by the retrograde injection of contrast medium through a catheter passed up from the femoral artery affords a high degree of accuracy in confirming or excluding a clinical diagnosis of dissecting aneurysm. In 3 cases of suspected acute aneurysm the diagnosis was confirmed and in 3 others it was considered erroneous.

Of 6 cases described and illustrated the aneurysm involved primarily the thoracic aorta in 4, the lumbar aorta in one, and the common iliac artery in one. Characteristically the contrast medium showed the true lumen of the vessel to be compressed and somewhat twisted and in some cases the extra lumen of the aneurysm was visualized. This radiological delineation of the extent of the aneurysm may be of great value in surgical treatment. *A. M. Rackow*

1352. **Aortic Configuration in Congenital Heart Disease**

E. C. KLATTE, J. A. CAMPBELL, and P. R. LURIE. *Radiology* [*Radiology*] **74**, 555–566, April, 1960. 14 figs., 16 refs.

The identification of congenital heart diseases by plain radiography is difficult but is often easier if attention is paid to the shape of the aortic arch. The authors have studied the angiocardiograms of over 600 patients seen at Indiana University Medical Center, Indianapolis, and

applied the findings to interpretation of the plain radiographs.

The appearances of the aorta in patent ductus arteriosus are well known and the authors demonstrated the infundibulum in 23 out of 100 cases. The point is made that in pulmonary hypertension with patent ductus the aorta will be small if the hypertension is due to the foetal type of pulmonary vasculature. In ventricular septal defect the size of the aortic arch is inversely related to the size of the left auricle, and it is also small in atrial septal defects and anomalous pulmonary veins.

Of 79 cases of Fallot's tetralogy in the series the aorta was large in 50 (63%). The aorta was also large in 12 (86%) of 14 cases of tricuspid atresia without transposition, while a small aorta was present in 3 out of 4 cases associated with transposition. In true truncus arteriosus the aorta is small except when the pulmonary vessels arise from the descending aorta, but these cases cannot be distinguished from those of Fallot's tetralogy. In transposition the aortic profile is small and often not visible. A small aorta is usually present in pulmonary stenosis and is a valuable diagnostic feature in distinguishing this condition from Fallot's tetralogy. Dilatation of the ascending aorta in aortic stenosis is well known, as also the small aorta of fibro-elastosis and the double knuckle of coarctation. *D. E. Fletcher*

1353. **A New Approach to Percutaneous Subclavian Angiography**

H. L. Baker Jr. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **35**, 169–174, March 30, 1960. 4 figs., 6 refs.

Angiographic visualization of the vertebral-basilar arterial system has become increasingly important in the last few years because of the interest in the diagnosis and surgical treatment of atherosclerotic disease of these vessels. As surgical correction is applicable only to stenoses at the origins of the vertebral arteries, angiographic methods to demonstrate these areas have received most attention. The present author describes a technique of injection of the subclavian artery percutaneously in the supraclavicular region about 2 inches (5·1 cm.) superior and lateral to the suprasternal notch. On the left side it is possible to puncture the common carotid artery near its origin and with a single injection demonstrate this vessel in its entirety, as well as the innominate, right carotid, and both subclavian and vertebral arteries. It is considered that this method of angiography in the study of patients with cerebrovascular disease has several advantages. It has been used in more than 60 consecutive cases without inducing pneumothorax, although this complication occurred twice in a series of 20 cases in which subclavian angiography was carried out, and is perhaps the only serious risk of the technique. It often affords visualization of all the vessels supplying the brain with only one or two arterial punctures instead of the three or four that are usually needed with other procedures.

[This technique should be of great value in demonstrating the extracranial portions of the vertebral arteries, and it is probable that it carries less risk of complications than direct puncture of the vertebral artery (see Morris, *Brit. J. Radiol.*, 1959, **32**, 673; *Abstr. Wld Med.*, 1960, **27**, 422).] *J. MacD. Holmes*

1354. **Pulmonary Veins in Rheumatic Heart Disease**

R. S. Ormond and A. K. Poznanski. *Radiology* [*Radiology*] **74**, 542–549, April, 1960. 12 figs., 16 refs.

The relationship between pulmonary vein size and left atrial pressure was studied at the Henry Ford Hospital, Detroit. Conventional postero-anterior chest radiographs of 172 patients who had undergone cardiac catheterization were examined and the size of the pulmonary veins was graded subjectively on a 1 to 3 scale by different observers. The left atrial pressure had been measured by percutaneous catheterization in 107 of the patients, but was not known when reading the plain radiographs.

A definite correlation was noted between the size of the veins and the pressure, the nature of the valve lesion having no effect. The upper lobe veins were found to be most reliable, the right upper lobe vein being fairly easy to locate where it crosses the right main bronchus. The lower lobe veins were disproportionately enlarged in the presence of congestive failure. *D. E. Fletcher*

1355. **Gas and Opaque Contrast in Roentgenographic Diagnosis of Pericardial Disease**

H. M. Stauffer, L. A. Soloff, J. Zatuchni, and B. L. Carter. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 1122–1126, March 12, 1960. 4 figs., 14 refs.

The relative merits in the study of pericardial disease of opaque and gas (carbon dioxide) angiography are discussed in this paper from Temple University School of Medicine and Hospital, Philadelphia. Animal experiments in which carbon dioxide was used for x-ray examination of the heart showed that the gas is harmless because of its high solubility in the blood, only transitory hypotension being produced. In adults rapid intravenous injections of 25 to 100 ml. of carbon dioxide has not caused any subjective discomfort. The patient is placed in the left-side-down position and the x-ray beam is horizontal. When the right atrium is filled with gas the lateral wall appears as a smoothly curved band, convex outwards, not more than 3 or 4 mm. thick. In the presence of a pericardial effusion a soft tissue shadow intervenes between it and the lung. The patient is kept in the left lateral position for 5 to 10 minutes after the last injection to avoid any possibility of embolism. The injection is given into the median antecubital vein, the needle being connected by a three-way stopcock to an intravenous drip. A 100-ml. syringe is flushed out with pure carbon dioxide and 100 ml. of the gas is rapidly injected; 100% pure carbon dioxide must be used. A radiograph is taken at the end of the injection and another one a few seconds later. Of 51 examinations carried out on 40 adult patients, positive evidence of pericardial effusion or thickening was obtained in 21 and negative or normal results in 18; the findings in 12 were considered to be equivocal. There were no untoward reactions.

The advantages of this technique over angiocardiography with opaque media are that it can be carried out with standard equipment, it causes the patient the minimum of inconvenience, and the possibility of reaction is less. On the other hand, although the carbon-dioxide technique will usually demonstrate a free pericardial effusion, it will not demonstrate one which is localized elsewhere than over the right atrial border; further it allows only a rough estimate of the size of the effusion and gives no indication of cardiac dilatation. In constrictive pericarditis, rigidity of the right atrial border can be demonstrated only by serial radiographs or cineradiography. The carbon-dioxide technique is of particular value in very sick patients or in those in whom only a cursory study of the pericardium is required.

John H. L. Conway-Hughes

1356. **Percutaneous Splenoportal Venography, with Additional Comments on Transhepatic Venography**
S. S. Zeid, B. Felson, and L. Schiff. *Annals of Internal Medicine* [*Ann. intern. Med.*] **52**, 782–805, April, 1960. 11 figs., bibliography.

The authors report from the University of Cincinnati College of Medicine, Ohio, their results in the performance of splenoportal venography on 50 occasions in 41 patients. In the main the examinations were carried out when considering surgery to relieve portal obstruction and in an attempt to determine whether the obstruction was intra- or extra-hepatic. In most cases intrasplenic pressure readings were made before the injection of the contrast medium. In the authors' experience contraindications to the procedure include inability of the patient to tolerate splenectomy, sensitivity to the drugs employed, the presence of renal disease or of local disease in the injection area, a tendency to bleeding, a low haemoglobin value, and any condition predisposing to splenic rupture. Three deaths occurred in this series, one in a seriously ill infant, a second due to splenic laceration in a 78-year-old man, and the third as a result of infection with *Bacillus welchii*. The detailed findings are tabulated.

Success was achieved on 42 of the 50 occasions, a success rate of 84%. The chief cause of failure on the other 8 occasions was injection of the medium extrasplenically or into the splenic capsule. There were no serious sequelae. Of 20 cases subjected to laparotomy at a later date an intraperitoneal haematoma was found in only 2; small intrasplenic infarcts or haematomata were found in the majority of the 12 spleens examined pathologically.

The radiological findings in intrahepatic and extrahepatic portal obstruction are discussed and contrasted, venograms illustrating both types being reproduced. Tumours, particularly those of the pancreas, are liable by their proximity to impress or distort the portal or splenic vein and one case of such distortion is illustrated. Secondary carcinoma in the liver may be revealed by the presence of translucencies in the hepatogram generally obtained in the later stage of the examination. In one case in this series the accidental injection of the left lobe of the liver gave rise to a hepatogram which revealed signs of pressure by a pancreatic tumour and metastases in the liver. This prompted a trial of this technique in 3 other cases with the result that in 2 of them secondary tumour nodules were identified. No evidence of permanent liver damage was found.

In discussing the findings the authors note that evidence of oesophageal or gastric varices was frequently obtained, although in 11 of these cases a barium swallow had failed to reveal them. Failure of the opaque medium to enter the liver did not always mean that there was extrahepatic portal block, since the venous back pressure from the liver might be great enough to deflect the stream via the collateral vessels. It is suggested that the technique is also of value in assessing the results of a portacaval shunt operation. In the authors' one case of this type the spleno-portal venogram showed a good anastomosis and no collateral circulation. *A. M. Rackow*

RADIOTHERAPY

1357. **Giant-cell Lesions of Bone. Osteoclastoma and Giant-cell Tumour Variants. Survey of a Radiotherapeutic Series**
J. Walter. *Clinical Radiology* [*Clin. Radiol.*] **11**, 114–124, April, 1960. 11 figs., 14 refs.

The results of irradiation in 14 cases of osteoclastoma, in 6 of which the diagnosis was proved histologically, are described in this paper from the National Centre for Radiotherapy, Sheffield. It is pointed out that there is no " typical " radiological appearance in osteoclastoma and that diagnosis of this condition in a patient under 18 years " must always be suspect ". The dosage in the present series varied between 2,000 r. in 3 weeks and 4,000 r. in 4 weeks; with supervoltage it ranged from 3,000 r. in 3 weeks to 5,100 r. in 4 weeks. Of the 14 patients, 9 made satisfactory clinical and radiological progress for 2 to 20 years. Good clinical but uncertain radiological progress were observed at 2 to 2¾ years in 3 patients while in 2 treatment failed and amputation was performed.

The author also describes 5 cases of simple bone cyst and fibrous dysplasia treated by irradiation with good results in one and no effect in the others. He advocates surgery in the treatment of giant-cell epulis, but has found irradiation to be of value in cases of aneurysmal bone cyst. Satisfactory regression was obtained with irradiation in 2 cases of benign osteoblastoma (giant osteoid osteoma). *M. Sutton*

1358. **A Wedge Filter Approach with 4 MV Radiation to the Treatment of Carcinomata of the Alveolus and Antrum**
J. G. Stewart. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **53**, 239–242, April, 1960. 6 figs., 3 refs.

In the treatment of carcinoma of the lower alveolus, antrum, and accessory sinuses the poor depth dose of conventional 250-kV. radiation and the loss of wedge angulation made the use of wedge filters a difficult physical problem. With the advent of 4-MeV. radiation attenuation of the primary beam, as for example by a wedge, is accurately reflected in the isodoses, so that the wedge angulation is maintained into depth. Correction

of the dose for tumours in or near the skin surface by the use of bolus becomes less essential, but is still important for tumours round the mouth. For centrally situated tumours "cross-fire" by plain fields is as efficient as two wedged fields, but for peripherally placed tumours wedge filters have great advantages in simplicity and economy of irradiation. Three wedges of different slopes—40, 50, and 60 degrees—are in current use, the optimum shape of the high dose zone and surface obliquity determining the choice of a particular wedge.

For anterior lesions of the lower alveolus radium moulds plus beam are still preferred, but for posterior alveolar lesions two wedged fields at 4 MeV. are used. The tongue may be displaced by a block of dental compound. Reactions are confined to one side of the mouth. The usual dose is 6,000 rads in 3 weeks. For neoplasm of the antrum or sinuses treatment is divided into two categories: (1) if the lesion is below the level of the roof of the antrum a wedge pair from the front and side gives adequate coverage, the upper level being just below the pupil of the eye; (2) if the orbit, ethmoids, and sinuses are involved, however, the upper limit is raised and a pair of anterior and superior wedge fields are used to avoid inclusion of the eye in the lateral field. Superficial effects on the cornea and conjunctiva are overcome by keeping the eye open. If a wax "build up" over the ethmoid region is used a peep-hole is preserved in front of the pupil in order to spare the cornea from the anterior field. The depth dose at 4 MeV. is independent of shape, and odd-shaped fields are permissible in special cases. In regard to dosage, if the treated volume "is less than a 7-cm. cube" 6,000 rads are given in 3 weeks; over this limit, 5,500 or 5,250 rads are given in 3 weeks, depending on size.

The results for two periods, 1950–4 and 1956–7, are compared. Of 108 patients with alveolar tumour treated in the earlier period 57% survived for 2 years and 45% were dead or had a recurrence; the corresponding figures for 21 similar cases treated by 4-MeV. wedge irradiation were 48% and 33%. Of 136 patients with involvement of the antrum and sinuses treated by the earlier methods 31% survived for 2 years and 60% were dead or suffered recurrence, compared with 38% and 47% respectively of 21 cases treated with MeV. for similarly situated lesions. *I. G. Williams*

1359. **Seminoma of the Testis**

R. Gibb. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **53**, 235–238, April, 1960. 6 figs., 1 ref.

Clinical experience and experimental work has suggested that the R.B.E. (relative biological efficiency) of 4-MeV. radiation is 85, compared with 100 for conventional 250-kV. therapy. A number of clinical trials contrasting 250 or 500 kV. with 4-MeV. therapy are now in progress.

In the present paper from the Christie Hospital, Manchester, the results of large field therapy of seminoma of the testis, taken as an example, are considered. Accepted practice at the Christie Hospital is based on the following principles: (1) the irradiated volume includes the scrotum and the inguinal, iliac, and para-aortic lymph nodes; the whole scrotum is irradiated because shielding may be only partial, with subsequent genetic risks, or the shield may slip over to the affected side and thus reduce the dose received there; (2) the volume to be treated should be irradiated in one block of tissue to avoid low dosage at gaps between the fields; (3) the volume should be irradiated as homogenously as possible. In using the 4-MeV. linear accelerator parallel opposed fields are employed. Any desired sizes are now available and irregular shapes can be obtained by interposing lead blocks in the beam. With the MeV. beam the depth dose is homogenous, so that the kidneys can be totally shielded while the para-aortic nodes receive high dosage. The upper margin is the xiphisternum, the lower edge the perineum. The width treated includes the iliac and inguinal lymph nodes, that is an area of some 800 to 900 sq. cm. with a focal skin distance of 130 to 150 cm. The total dose is 3,000 rads given over 4 weeks. The effects on the blood and bowel and general reactions appear the same as with 250-kV. irradiation. If metastases are present in the abdomen shielding of the kidneys may not be practicable and the dose is reduced to 2,000 rads in 3 weeks, by which time the tumour mass may have shrunk so that the kidneys can be shielded and the tumour dose raised to 3,000 rads. Pulmonary metastases are treated through two opposed fields to the chest, covering the lungs, mediastinum, and supraclavicular fossae, the dose being 2,500 rads over 4 weeks.

Results so far indicate that equal palliation can be achieved with 4-MeV. irradiation as was obtained with the earlier more complicated and time-consuming methods of treatment. *I. G. Williams*

1360. **Bladder Carcinoma**

R. C. S. Pointon. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **53**, 244–246, April, 1960. 1 fig.

At the Christie Hospital, Manchester, the 4-MeV linear accelerator came into routine use for the treatment of carcinoma of the urinary bladder in 1955; in this paper the various methods of treatment of this lesion are described. (1) Mucosal and muscular tumours up to 4 cm. in diameter are treated by radon seed implant. (2) Metastatic tumours and those with gross pelvic fixation were given only palliative therapy. (3) All others, including multiple mucosal recurrent or residual tumours received radical x-ray therapy, provided the patient's general condition permitted. Because of the limited radiosensitivity of tumours of the bladder the principle of "small volume, high dose" has been adhered to. Field sizes are 6×8 cm. for small lesions and 10×8 cm. for larger lesions. Location of the tumour is based on cystoscopic examination under anaesthesia and on the cystographic findings, using a weak barium suspension. In some cases inactive gold seeds were inserted cystoscopically to demarcate the limits of the tumour and this is undoubtedly the best method. The technique of treatment consists in a symmetrical arrangement of three fields, one anterior and two postero-lateral. The MeV. linear accelerator is so designed that it rotate

about a point one metre from its focal spot, so that it acts as its own pin and arc. The dose for fields with an area up to 50 sq. cm. is 6,000 rads, and for those up to 80 sq. cm. 5,500 rads in 3 weeks.

The results for the years 1953–4 are compared with those for 1955–6 when megavoltage therapy came into use. Among 97 patients treated by radical x-ray therapy the 3-year crude survival rate was 27%, compared with 29% of 87 treated by MeV. Symptoms due to bladder reactions during therapy have not been severe. A few cases did, however, develop rectal reactions and one patient died from necrosis of a small area of pelvic colon and peritonitis. Late bladder complications have not been seen. In 1957, with the acceptance of a "relative biological efficiency" (R.B.E.) ratio of 85:100 the dose has been increased to 6,000 or 6,500 rads in 3 weeks, depending on field size. No significant increase in severity of symptoms has been noted. In order to compare the results of 4-MeV. treatment with those of 500-kV. x-ray therapy a clinical trial, with strictly random selections of patients, is now being conducted but is still too recent to be reported on. *I. G. Williams*

1361. **Carcinoma of the Bladder: Its Treatment by Supervoltage X-ray Therapy**
R. MORRISON. *Clinical Radiology* [*Clin. Radiol.*] **11**, 125–129, April, 1960. 2 figs., 12 refs.

The author of this paper from the Medical Research Council Radiotherapeutic Research Unit, Hammersmith Hospital, London, describes the treatment of 210 patients with carcinoma of bladder by the 8 MeV. linear accelerator. Usually 4 obliquely directed fields were employed; occasionally the author used a 3-field technique (with a single anterior central field) or 2 anterior oblique fields with wedges. The average field size for intravesical lesions was 7×9 cm. and the tumour dose was 5,500 rads in 4 weeks. For extravesical tumours the factors were: a field size of about 10×10 cm. and a tumour dose of 4,500 rads in 4 weeks. Cystograms were taken to assist planning. Anaemia and infection were treated before irradiation and a low residue diet was given during treatment. In some patients frequency of micturition developed from fibrous contraction of the bladder, but this tended to improve after a few months.

Cystoscopy performed a few weeks after treatment showed complete regression in 64 patients (31%), partial regression in 35 (17%). Haematuria usually ceased after the third week of treatment. The 2-year survival rate in the series was 35%; it was 44% in patients with intravesical tumours (T1 and T2) and 26% in those with extravesical lesions (T3 and T4). *M. Sutton*

1362. **The Treatment of Inoperable Cancer of the Biliary System with Radioactive (I^{131}) Rose Bengal**
I. M. ARIEL and G. T. PACK. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **83**, 474–490, March, 1960. 8 figs., 16 refs.

The organic dye rose bengal is rapidly concentrated by the liver and excreted into the biliary system. It seemed plausible to the authors that if the dye were iodinated with radioactive iodine (^{131}I) the gamma rays emitted might damage or destroy a neoplasm in the biliary tract. With this in mind they have therefore investigated the effect of rose bengal containing ^{131}I in 14 patients with inoperable cancer of the biliary system. The dose varied from 10 to 31 mc. and was given intravenously by a remote-control method. Half the dye was given rapidly (to saturate the excretory mechanism) and the other half over 3 to 5 hours.

Of these 14 patients 12 died of their cancer within 6 to 24 months, the average duration of life being 8 months; only a short follow-up was possible in the other 2 cases. Over-all there was no benefit in 5 cases but some palliation in 7, while complications occurred in 2 cases, these consisting of paraesthesiae in the feet in one and bilateral foot drop in the other. Hepatic scintigrams, performed on 3 patients, showed that there was good dye concentration in one case and this was associated with good clinical response, but the other 2 cases showed poor concentration and no clinical benefit. *M. Sutton*

1363. **The Effect of Radiation upon the Heart**
M. CATTERALL. *British Journal of Radiology* [*Brit. J. Radiol.*] **33**, 159–164, March, 1960. 7 figs., 6 refs.

The effect on the heart of radiation to the chest was studied in 26 patients at the London Hospital. Full clinical, radiological, and electrocardiographic (ECG) investigations were carried out before radiotherapy and for one year afterwards. In a group of 5 men and one woman with inoperable carcinoma of the bronchus, a telecobalt-60 unit delivered a tumour dose of 4,000 rads in one month by two fields of an area of 150 sq. cm. Radiographs showed that the great vessels rather than the myocardium received this dose. No ECG changes were observed. Irradiation of the chest wall and lymph-node areas was carried out following mastectomy in 20 women with carcinoma of the breast, the factors being 250 kV. with 1 mm. copper filter and a half-value layer of 1·74 mm. copper, delivering a tumour dose of 3,650 r. in 3 weeks. The chest wall and internal mammary glands were treated by medial, lateral, and inferior glancing fields. The position of the heart in relation to these fields was obtained by radiographic studies with lead skin markers; the dose to the heart was calculated at 9 points. Less than 1,000 r. was received by the heart in the 8 patients who had irradiation of the right chest wall and 3 of the 12 patients who had irradiation of the left side. The ECG in these cases was normal throughout. In the remaining 9, part of the heart was irradiated to 2,200 to 3,200 r. and all showed abnormal T waves in Leads 1 and CR4. This localized the myocardial injury to the left ventricle, as would be expected from the radiation technique employed. These changes were present 4 months after treatment but had disappeared 8 months later.

Dissection of the thorax demonstrated the close relationship of the internal mammary glands to the heart. A portion of lung interposed would protect the heart from irradiation. Pulmonary function studies showed no relationship between myocardial and lung damage.
M. B. Duthie

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